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THIRD SERIES FOUNDED BY EDWARD JACKSON

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DEPARTMENTS

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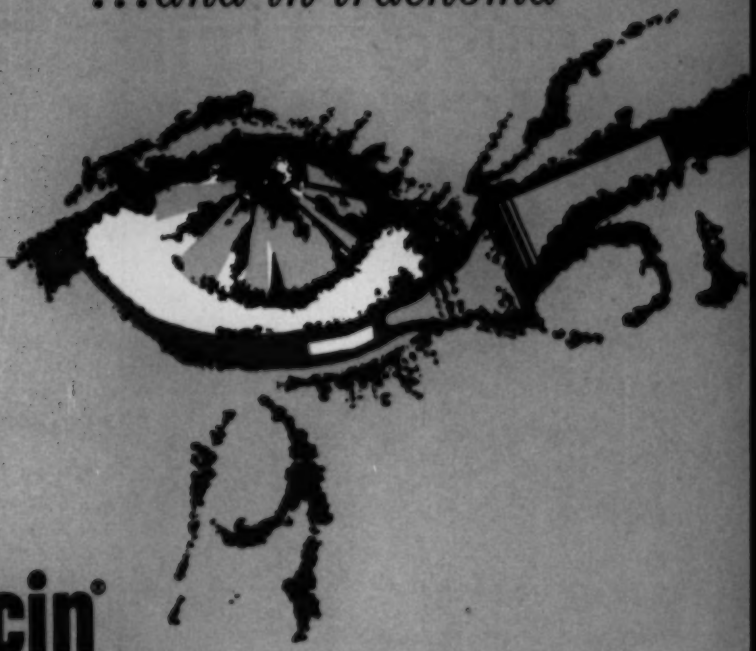

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1. Gordon, D. M., and Ehrenberg, M. H.: Am. J. Ophth. 38:831 (Dec.) 1954.

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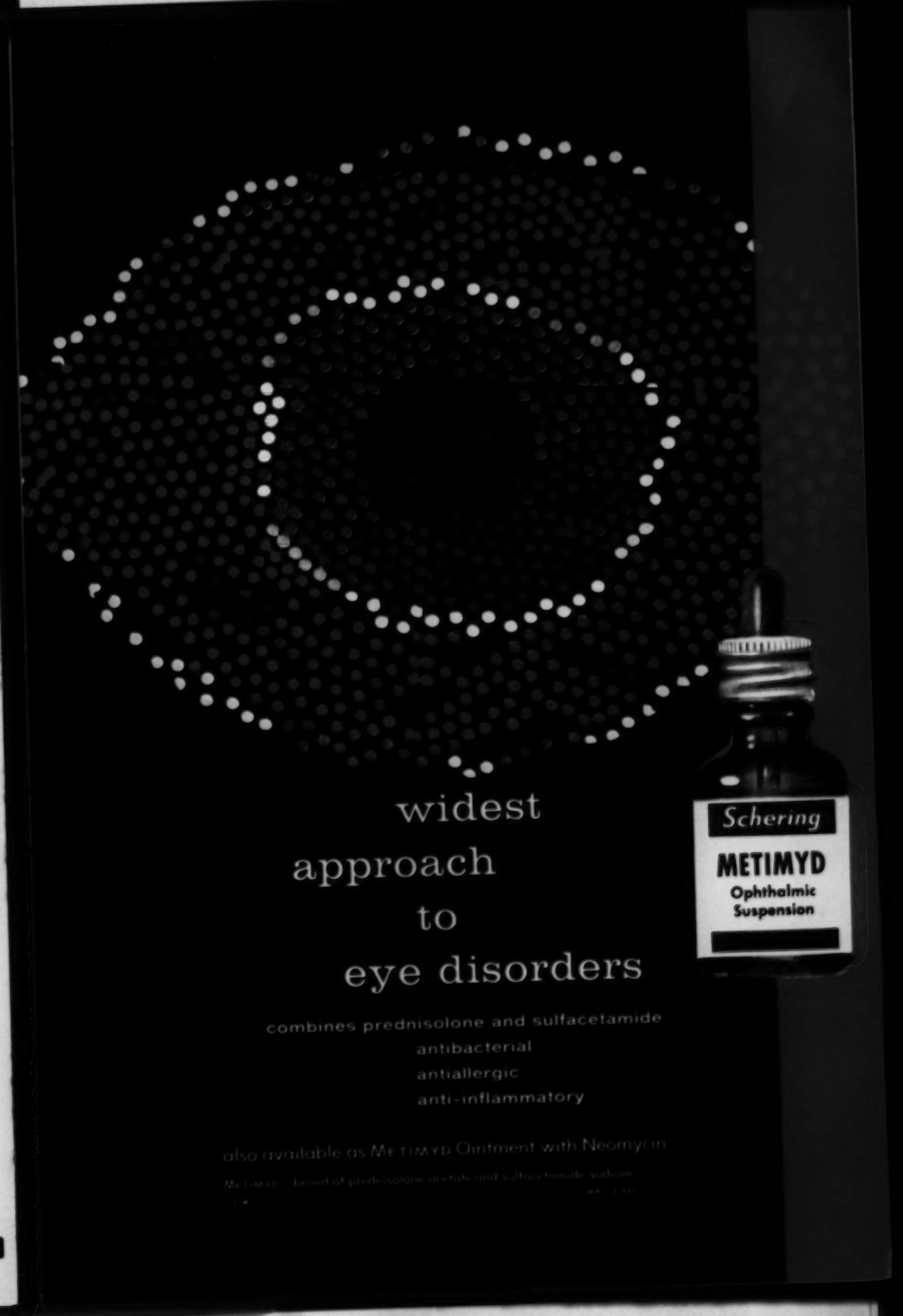
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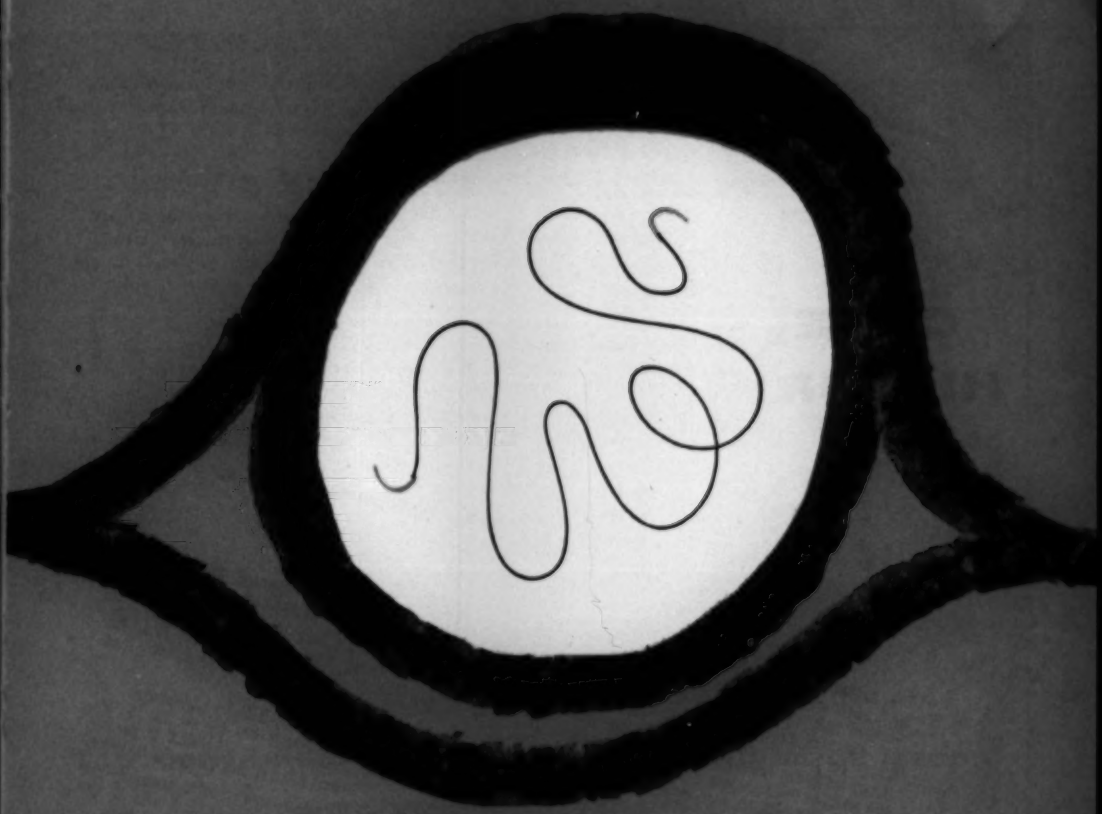

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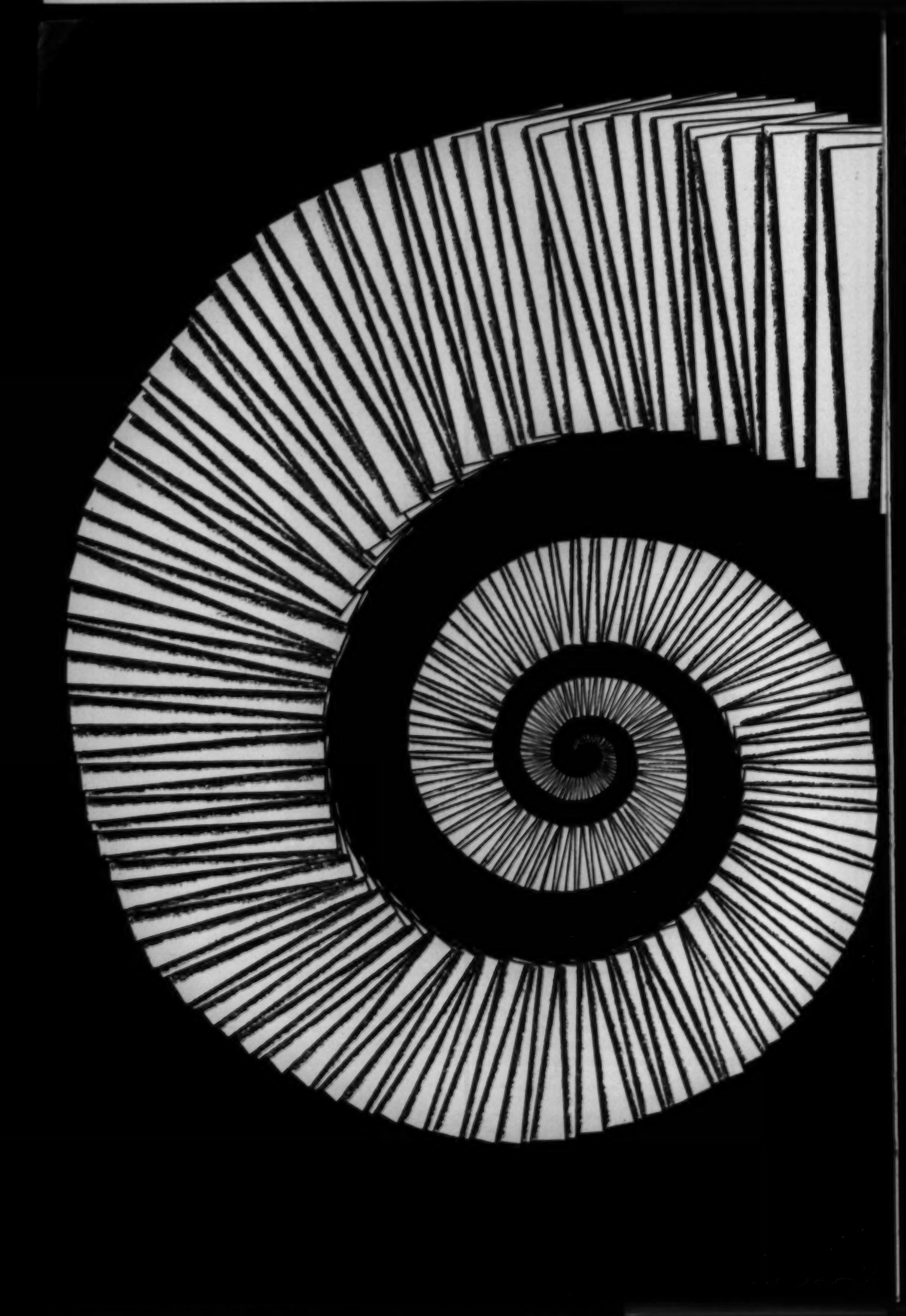

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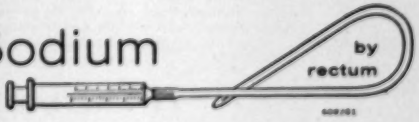

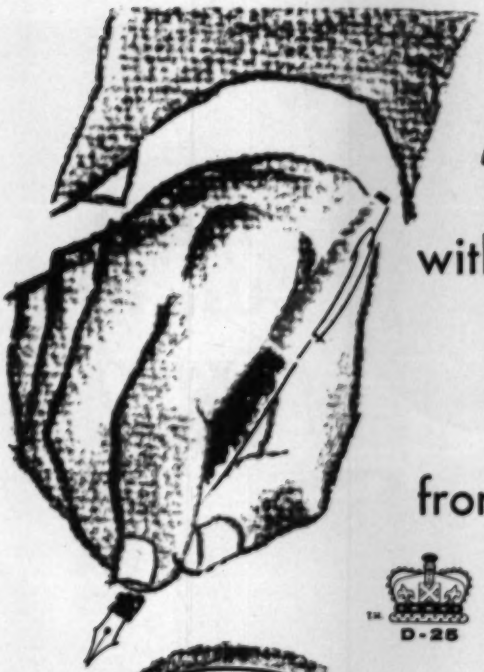

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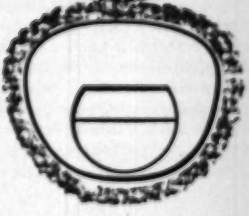

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AMERICAN JOURNAL OF OPHTHALMOLOGY

VOLUME 42 AUGUST, 1956 NUMBER 2

EXPERIMENTAL STUDIES ON A SCLERAL BUCKLING OPERATION*

ANGELOS DELLAPORTA, M.D.
Buffalo, New York

In the decade which followed the report in 1933 of the greatly improved technique of penetrating scleral resection operation by Lindner,[1,2] only few such operations were performed outside Vienna (Pischel,[3,4] Vail[5]). This is probably attributable to two factors: The operation is technically difficult, time-consuming, and not without dangers to the eye in hands not specifically trained. On the other hand, at this period ophthalmologists were occupied in acquiring experience with the then relatively new but nowadays conventional diathermy operation.

After World War II more surgeons performed the operation, but it became popular only after the simplified technique of lamellar scleral resection was introduced. Lindner was the first to suggest the lamellar scleral resection in his original paper in 1933. He performed the operation in six cases in 1946,[6] but he later found that in some cases which had to be reoperated he had not obtained a permanent shortening of the eyeball.[7]

The failures were most probably coincidental because later experimental and clinical work proved that both operations, the penetrating scleral resection and the lamellar scleral resection, have identical curative effects for selected cases of retinal detachment (Friemann,[8] Dellaporta,[9,10] Paufique and Hugonnier,[11] Shapland[12,13]). Both operations effect a mechanical shortening of the sclerochoroidal capsule bringing the choroid nearer to the detached retina. In addition, the penetrating scleral resection produces an extended mild inflammation of the choroid around the scleral wound, which is missing after lamellar scleral resection but which is successfully induced by diathermy application, as clinical experience shows. The mechanical shortening of the sclera in both operations is permanent but the general experience is that the sclera stretches slowly so that the final shortening of the eye, months or a year after the operation, is less than that found immediately after.

A related procedure, the scleral folding, was suggested by A. Vogt[14] in 1933. He stated that, if the retina does not flatten after drainage of the subretinal fluid, this is due to a surface shrinkage of the vitreous adhering to the retina. For such cases he recommended "to shorten the surface of the sclera by producing a scleral fold by means of three to four sutures." The same principle was applied later by Weve[15,16] in his technique of "reefing" of the sclera: A running catgut suture placed intrasclerally in meander form produces, when tightened, a six to seven mm. wide infolding of the sclera in meridional or equatorial direction and therefore a shortening of the scleral wall. Where lasting shortening is desired a strong nonabsorbable suture material is used. Weve performs his method combined with diathermy applied over the retinal break.

* From the Buffalo Eye Bank and Research Laboratory, University of Buffalo Medical School. This study was supported by the Arnold Reuben Fight for Sight Fund of the National Council to Combat Blindness.

Another type of operative procedure relative to those mentioned above is that reported by Jess in 1937.[17] After diathermy application around the retinal break and drainage of the subretinal fluid he produces an artificial indentation of the sclera over the detached retina by a tightly folded gauze pad applied on the sclera for 14 days. The indentation of the sclera pushes the choroid nearer to the detached retina and facilitates its reattachment. He uses this technique for detachments with high elevation of the retina.

Custodis[18,19] uses a similar principle: The common postoperative hypotony found after diathermy application and the drainage of the subretinal fluid in retinal detachment operation induced him to produce an indentation of the sclera overlying the retinal break. The indentation is achieved by infolding the sclera and keeping it in that position with the help of a cylindrical piece of "poliviol" inserted in the scleral groove and fixed by strong intrascleral "supramid" sutures. Poliviol is a polymerized alcohol with elastic, rubberlike consistency and chemically inert to the tissue. Supramid is a strong chemically inert synthetic suture material.

The indented sclera pushes the choroid nearer to the retina and facilitates reattachment. The higher the elevation of the detached retina, the more subretinal fluid is drained; therefore the hypotony is more pronounced and the scleral indentation is deeper. The poliviol cylinder is left in place indefinitely, or is removed in a few cases two to six weeks after surgery if the surgeon deems it desirable, or in case of undue eye irritation.

Custodis at first reserved this method for selected cases, that is, balloon detachments, detachments with giant breaks, and so forth, but later he used it for every detachment case. Between 1949 and 1953[19] he operated 340 cases with this method. He claims that his procedure enables considerable shortening of the average hospitalization for retinal detachment surgery. No bedrest is ordered preoperatively to flatten high detachments. The first days after surgery the fundus is examined and as soon as the retina is found to be attached to the protruding choroid, the patient is allowed out of bed with stenopaic glasses. This happens in uncomplicated cases in two to three days, in complicated cases in five to eight days after surgery.

Schepens[20] reported a similar method which he calls scleral buckling, and which consists basically of the following: "Diathermy applications of the sclera overlying the retinal breaks, release of subretinal fluid, and infolding of the treated sclera and choroid. The immediate result of the last step should be either to close the retinal breaks or to wall them off." He prevents the infolded sclera from collapsing by inserting permanently within it a tube of polyethylene, though he did not mention this particular in his discussion remarks. The results of the last two procedures seem to be encouraging, especially in cases which would have unfavorable prognosis if operated with conventional diathermy applications.

The procedures of Custodis, and Schepens have in common that the sclerochoroidal wall overlying the retinal breaks is temporarily or permanently indented in order to facilitate reattachment of the separated retina to the artificially inflamed choroid.

In the following experiments a type of permanent scleral buckling operation was performed on normal dogs' eyes in order to obtain information about the histologic changes occurring after this type of operation. No diathermy applications were applied in order to obtain the clear effects of the operation.

Technique

Twenty-eight normal eyes from dogs weighing 10 to 20 kg. were used for the experiments. After general anesthesia with intravenous pentobarbital (Nembutal) and retrobulbar injection of 3.0 cc. of two-

percent procaine hydrochloride, a five to six cm. long temporal (posterior) canthotomy was performed and the crescent-shaped cartilage forming the temporal margin of the orbit was cut through with heavy scissors at the level of the canthotomy; this facilitated the exposure of the temporal wall of the eye.

The sclera was freed from conjunctiva and episcleral tissue, the lateral rectus temporarily separated from its insertion, and a traction suture passed through both the superior and inferior recti. These traction sutures and a U-shaped catgut thread placed in the sclera through the insertion of the lateral rectus, and armed with medium sized hemostats, secured a satisfactory exposure of the temporal half of the sclera.

The equatorial strip of sclera which was to be infolded was then outlined with the lancet caliper (fig. 1-A) eight to nine mm. posterior to the limbus. In 14 eyes in which the inserted polyethylene tube was two mm. in the external diameter the scleral strip was five-mm. wide; in the remaining 14 eyes in which the inserted polyethylene tube was one-mm. in diameter the strip was three-mm. wide. The length of the scleral strip covered approximately half of the circumference of the globe, and in the eyes with the two-mm. tube slightly less.

Six to eight nonabsorbable 3-0 silk mattress sutures were placed as shown in Figure 1-B with 2.0 to 2.5-mm. wide intrascleral bites to secure a good holding in the scleral tissue. The polyethylene tube, sterilized in 1:1,000 Zephiran solution and washed in one-percent saline solution, was slipped under the sutures (fig. 1-C). After the intraocular pressure had been lowered by tapping the anterior chamber through a paracentesis, the silk sutures were tightened and knotted in sequence.

During this procedure the sclera infolded and the tube was gradually buried within the fold as shown in Figure 1-D. The ends of the tube were cut in a slanted direction and buried within the fold with two additional single silk sutures. After tightening the sutures the folded "scleral wound lips"* were in good apposition in the eyes with the one-mm. tube, whereas they were 1.0 to 1.5 mm. apart in the eyes with the two-mm. tube. There was some deformity of the eye after the operation especially in the cases with the two-mm. tube.

Finally, the lateral rectus was sutured and the wounds of the conjunctiva and the canthotomy were repaired and 20,000 units of aqueous penicillin were injected subconjunctivally.

The surgically treated eyes were enucleated at times varying from several minutes up to six months after operation and the specimens were examined histologically.

A. Ophthalmoscopic findings

Immediately after the operation, a cylindrically shaped protrusion of the dark pigmented choroid and the overlying retina was observed along the infolding of the sclera. The protrusion was higher (deeper) in the eyes with a two-mm. polyethylene tube, but exact measurement was not possible because the basis of the protrusion was not visible with the ophthalmoscope. In most instances meridional rippling of the retina was observed on the summit of the protrusion usually around the horizontal meridian, especially in eyes with the two-mm. tube, and the retina appeared there to be slightly detached. Both the rippling and the detachment of the retina diminished gradually toward both ends of the protrusion.

In the following days no noteworthy change occurred in the fundus picture except that the chorioretinal protrusion appeared to be appreciably lower in the eyes containing the one-mm. tube. Three weeks after the operation the retina seemed to have reattached to the choroid over the protrusion

* In the following description the term "scleral wound lips" is used for the outer opening of the scleral fold which is held together by the sutures over the polyethylene tube though it actually does not represent a real wound.

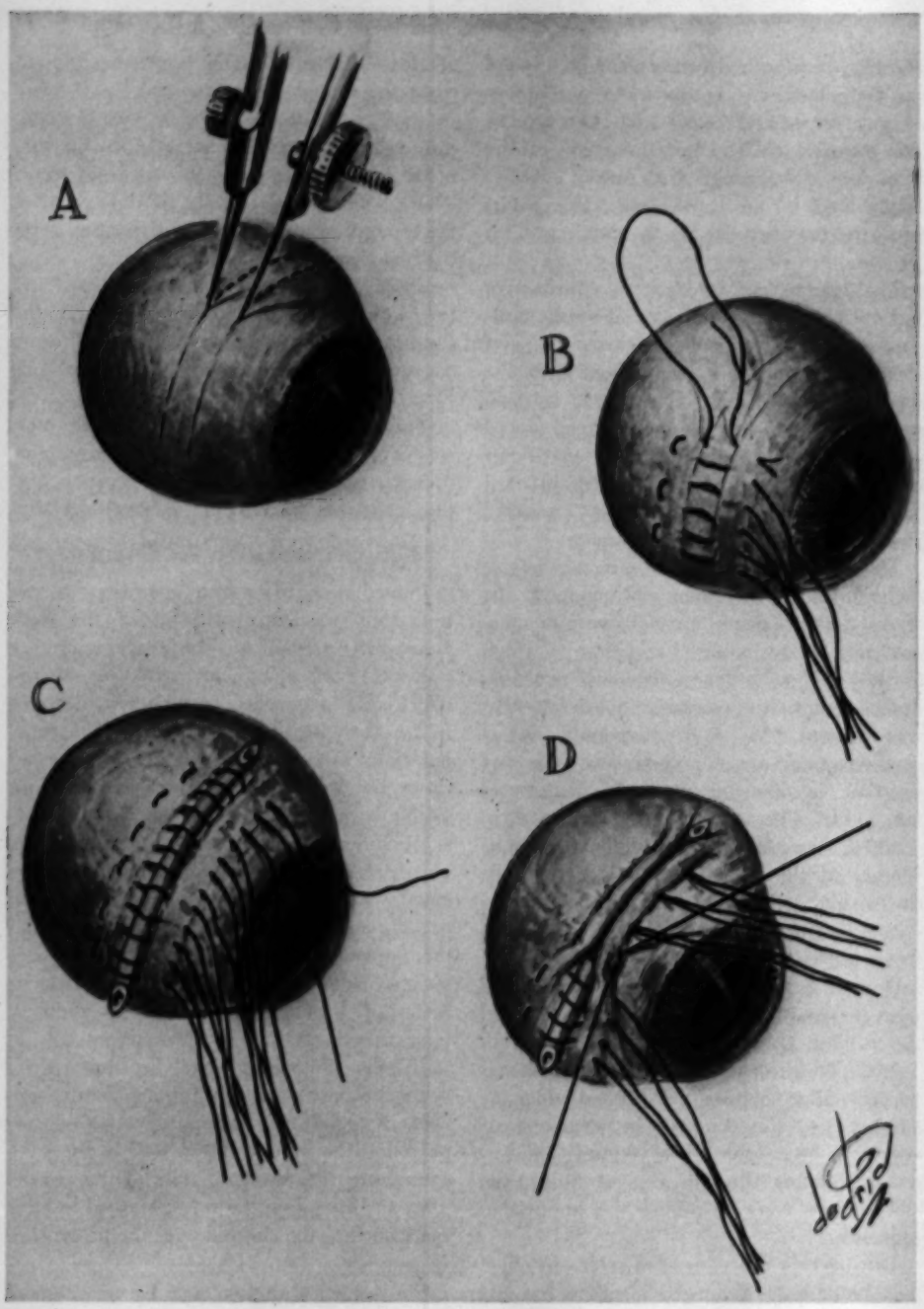

Fig. 1 (Dellaporta). Four steps of the scleral buckling operation. (A) Outlining the scleral strip which is to be infolded. (B) Insertion of sutures. (C) The polyethylene tube is slipped under the sutures. (D) By tightening the sutures the "wound lips" approximate and the tube is buried within the scleral fold.

and the retinal rippling was hardly discernible with the ophthalmoscope. By that time the chorioretinal protrusion in the eyes containing the one-mm. tube had flattened considerably so that thereafter it was only recognizable as a flat gently sloping unevenness of the interior of the eye. However, the protrusion in the eyes operated with the two-mm. tube did not change appreciably during the six-month follow-up period.

B. Anatomic findings

1. *Macroscopic study.* After fixation in 10-percent formalin, the eyes were sectioned on a meridional plane four to five mm. above the horizontal meridian, and the interior of the eyes examined with a magnifying loupe.

Immediately after the operation the infolded coats of the eyeball and the enclosed tube produce a spindle-shaped protrusion in the interior of the eye lying just behind and parallel to the ora serrata. For obvious reasons the eyes with the two-mm. tube show a wider and higher protrusion than those with the one-mm. tube but the difference is not as much as one would expect owing probably to the fact that the swollen and inflamed tissue surrounding the tube plays some role in bringing about the protrusion (fig. 2). In the weeks following the operation no appreciable change occurs in the size of the protrusion. However, two months after the operation and therafter, the eyes containing the one-mm. tube show the protrusion to be one third to one half the height found immediately after operation; whereas, the protrusion of the eyes with the two-mm. tube shows no appreciable change in size in the follow-up time of six months.

Immediately after surgery numerous meridional folds (rippling) are visible on the retina covering the sclerochoroidal protrusion and one to three equatorial retinal folds are seen along the posterior slope or the posterior foot of the protrusion (fig. 2). In contrast to the regular, short, flat meridional folds the equatorial folds are higher,

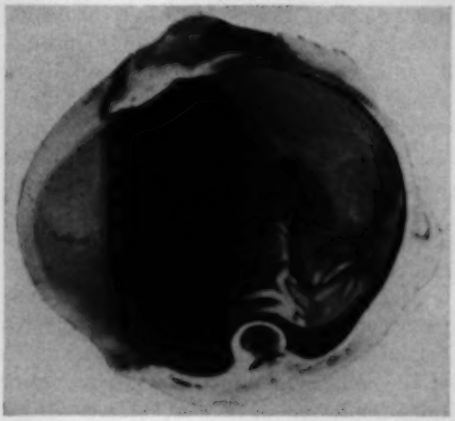

Fig. 2 (Dellaporta). Interior of an eye (#24R) in which a two-mm. tube was inserted, three days after surgery. Note the cylindrical protrusion into the interior of the eye. Over the protrusion the retina shows many meridional and some equatorial folds. Fine rippling of the retina between protrusion and optic nerve. Photograph was taken after fixation in 10-percent formalin.

much longer, and are occasionally interrupted. In the following three weeks no appreciable change occurs in the folds. After that time the equatorial folds begin to become lower and break down in smaller sections assuming the appearance of a chain or braid; six weeks after the operation these folds have practically disappeared. The meridional folds remain almost unchanged until six weeks after surgery, but begin thereafter to become gradually lower, finer, and less numerous, though still visible in the six-month follow-up.

In 14 out of 17 eyes which were enucleated within three weeks after surgery, fine multiple retinal rippling is seen between the protrusion and the optic nerve, or around the optic nerve, or near the ora serrata in the half of the globe lying opposite the operation area (fig. 2).

2. *Microscopic study.* After the embedding of the specimens in celloidin and before the sectioning, the polyethylene tube was carefully removed so as not to interfere with the preparation of thin sections.

Sclera. The anatomic relation of the three

membranes of the eyeball after the scleral buckling operation is shown in Figures 3, 4, and 5. The sclerochoroidal wall, lying tightly around the polyethylene tube, forms a cylindrical protrusion into the interior of the eye along the operated area. The retina follows in general the protruding choroid.

Immediately after the operation the scleral wound lips appear in good approximation in the eyes with the one-mm. tube, whereas in the eyes with the two-mm. tube the wound lips are gaping as already pointed out in the description of the operation.

The inflammatory reaction of the sclera following the operation is mild. Twenty-four hours after surgery small collections of leukocytes mixed with fibrin appear between the scleral wound lips. The scleral tissue around the operation area shows some swelling and diffusely scattered leukocytes. Some of the scleral fibers around the tube and the silk threads show homogenization and have lost their nuclei; these changes represent damage of the scleral tissue caused by the pressure of the foreign material and have been observed also after lamellar scleral resection (Dellaporta[9, 10]). In the remaining scleral fibers enveloping the tube diffusely scattered leukocytes are visible.

In the following two days more scleral fibers show homogenization and loss of nuclei (fig. 6) especially those fibers enveloping the tube, and the leukocytic infiltration is in most cases slightly increased. However, the degree of these changes could not be consistently related to the time lapsed

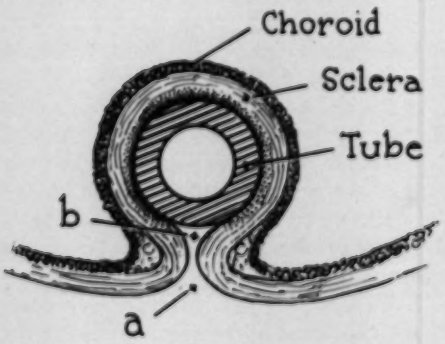

Fig. 3 (Dellaporta). The relation of the membranes of the eye around the tube. The retina is not shown. (a) Outer edge of the wound. (b) Inner edge of the wound.

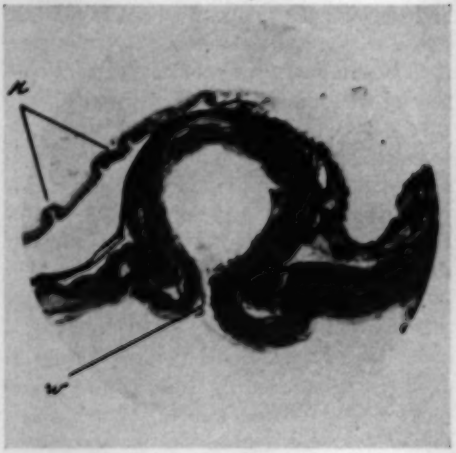

Fig. 4 (Dellaporta). (#25R) Operation area immediately after scleral buckling operation with one-mm. polyethylene tube. The tube has already been removed. (w) Well-adapted scleral wound lips. (r) Several equatorial retinal folds. The choroid closely follows the sclera.

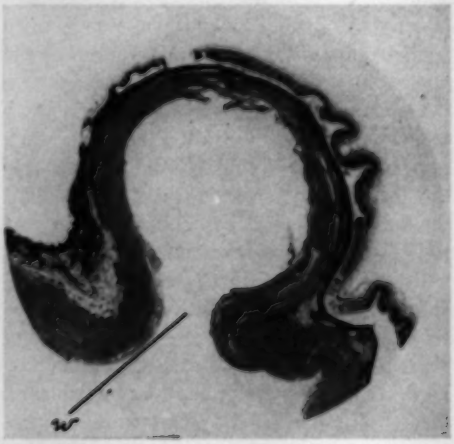

Fig. 5 (Dellaporta). (#24L) Operation area immediately after scleral buckling operation with the two-mm. polyethylene tube. (w) Gaping scleral wound lips. Anatomic relation of the membranes of the eye as in Figure 4.

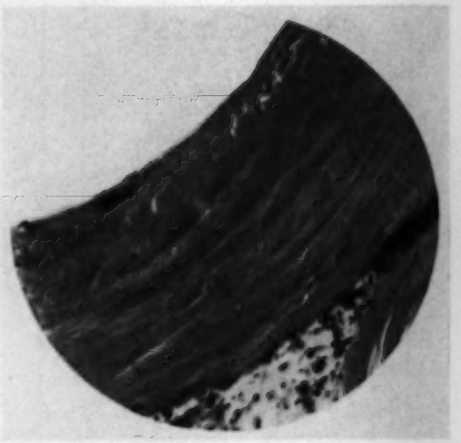

Fig. 6 (Dellaporta). (#23R) Four days after operation. Portion of the sclera which envelops the tube. Note homogenization of the scleral fibers and disappearance of the nuclei.

between operation and enucleation; it seems that the reaction of the individual animal plays a prominent role.

Three to four days after surgery the small or large dehiscences (depending on the tube used) of the scleral wound lips are plugged by a mixture of leukocytes, other inflammatory cells and fibrin fibers, the latter mostly arranged in a meridional direction (figs. 7 and 8). In the next days fibroblasts appear there forming a granulation tissue which slowly becomes fibrotic so that nine to 10 days after surgery the wound lips are closed by a young connective tissue containing varying numbers of inflammatory cells, several foreign body giant cells and many capillaries (figs. 9 and 10). This young connective tissue invades the adjacent fibers of the scleral wound lips, and in the area of the inner edge of the wound proliferates anteriorly and posteriorly over the tube in a crescent-shaped structure—in the meridional sections—whose inner lining consists of a membranelike layer of flattened fibroblasts (figs. 10 and 11). This lining lies directly on the tube and its formation seems to be induced by the smooth, nonirritating, chemically inert surface of the polyethylene.

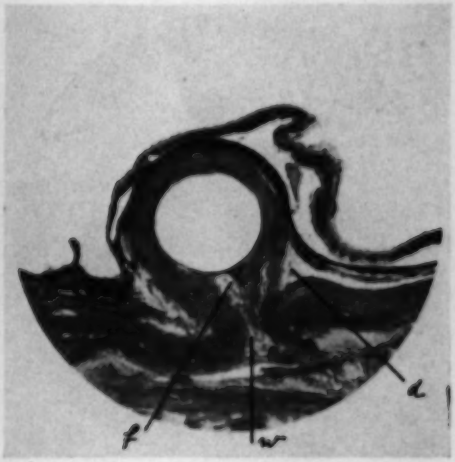

Fig. 7 (Dellaporta). (#23L) Operation area three days after surgery with the one-mm. tube. (w) Well-adapted scleral wound lips. (f) Accumulation of leukocytes and fibrin in the inner edge of the wound. (d) Localized detachment of the choroid from the sclera at the anterior foot of the protrusion.

In the scleral fibers enveloping the tube scattered leukocytes are seen in addition to the fibroblasts.

In the following days the connective tissue

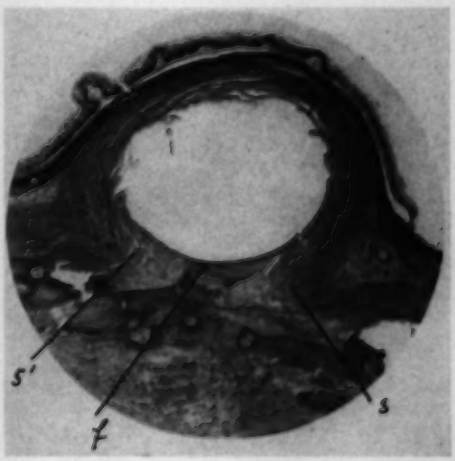

Fig. 8 (Dellaporta). (#14L) Operation area four days after surgery with the two-mm. tube. (ss') gaping scleral wound lips. (f) Fibrin and leukocytes fill the dehiscent wound lips.

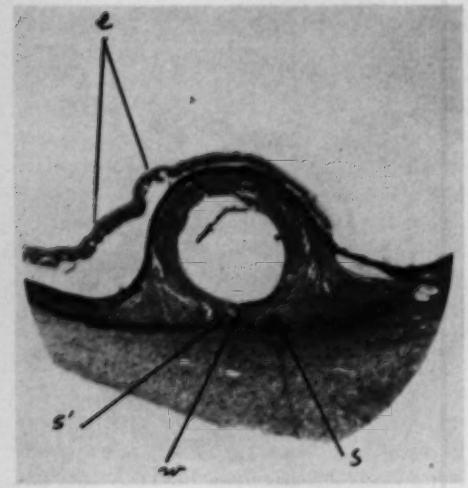

Fig. 9 (Dellaporta). (#17R) Operation area 10 days after surgery with the one-mm. tube. (ss') Scleral wound lips. (w) The wound is closed by fibrotic granulation tissue. (e) Several small empty spaces in the outer nuclear layer of the retina formed through necrosis and subsequent absorption of the nuclei caused by the sudden bending of the retina at the summit of the folds during the operation.

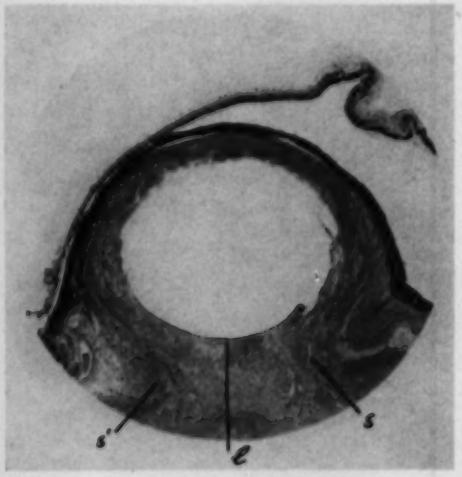

Fig. 10 (Dellaporta). (#22R) Operation area 10 days after surgery with the two-mm. tube. (ss') Scleral wound lips connected by fibrotic granulation tissue; the latter is lined against the tube by a membranelike layer (l) of flattened fibroblasts.

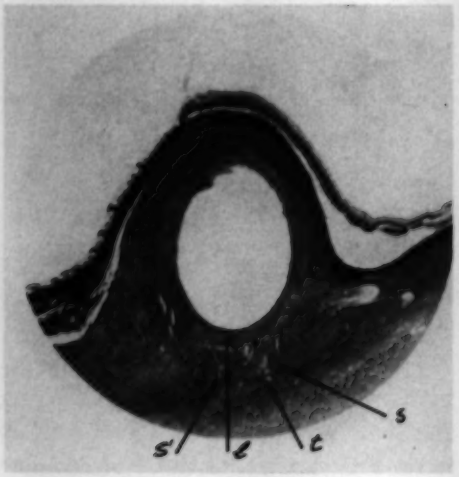

Fig. 11 (Dellaporta). (#19L) Operation area 20 days after surgery with the one-mm. tube. (ss') Scleral wound lips. (t) Dense connective tissue closing the wound. (l) Membranelike layer of flattened fibroblasts.

closing the wound matures, and the inflammatory cells disappear so that three weeks after surgery the scleral wound appears firmly closed by a tissue very similar to the surrounding normal sclera except that it contains more nuclei (fig. 11).

In the next weeks the connective tissue closing the wound becomes slowly identical to the surrounding normal tissue of the sclera (fig. 12). At the end of the six-month follow-up period the tube appears enclosed between the sclera and the postoperatively formed collagen tissue (figs. 14 and 15). Between tube and enveloping sclera a very thin lining layer of compressed fibroblasts is found (fig. 13); in addition most eyes show there small nests of encapsulated granulation tissue containing many round cells, tissue identical to that found around the silk sutures (figs. 12 and 14). Both changes represent a mild foreign body reaction and will probably persist for a long or even indefinite period of time.

The portion of the sclera enveloping the tube appears histologically normal at the

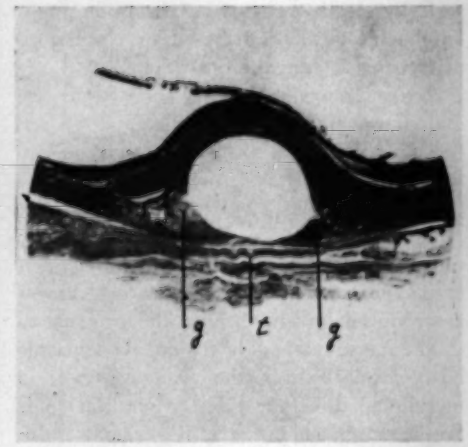

Fig. 12 (Dellaporta). (#12L) Operation area two months after surgery with the one-mm. tube. (t) The tissue closing the wound lips is identical to the surrounding sclera. (g) Nests of granulation tissue between tube and sclera.

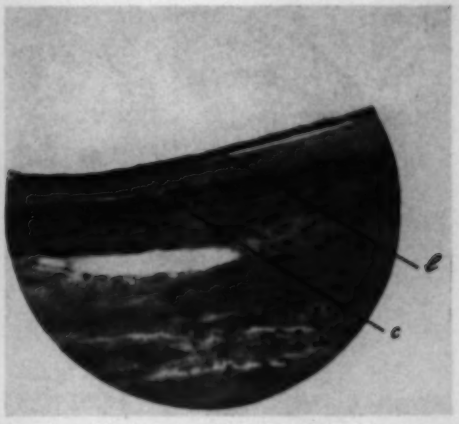

Fig. 13 (Dellaporta). (#11R) Case six months after surgery. The picture shows the final appearance of the newly formed collagen tissue (c) closing the wound, lined against the tube by the membranelike layer (l) of the flattened fibroblasts.

end of the six-months follow-up, though about one-third to one-half thinner than originally (figs. 14 and 15). The final degree of the sclerochoroidal protrusion is less than that found immediately after surgery so that in the eyes with the one-mm. tube the unevenness of the inner wall of the eye is slight (fig. 14); whereas, in the eyes with the two-mm. tube it is considerable, measuring 1.0 to 2.0 mm. in height (fig. 15). This decrease of the original protrusion is due to the tendency of the sclera to reassume its normal shape and size, a tendency observed also in other eye-shortening operations.

The histologic changes around the silk sutures are the same as those found after experimental scleral resection and are described in detail in a previous paper.[22]

Uvea. The ciliary body and the choroid lying in the half of the eyeball in which the operation is performed begin immediately after surgery to swell and to become markedly hyperemic. At the same time scattered leukocytes, some blood, and albuminous fluid appear in the subchoroidal space. These inflammatory signs increase in intensity quite rapidly and reach their peak

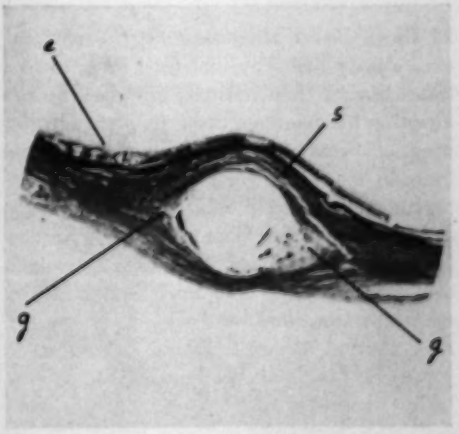

Fig. 14 (Dellaporta). (#16R) Operation area four months after surgery with the one-mm. tube. The latter is well enclosed between the sclera and the postoperatively formed collagen tissue. (g) Small nests of granulation tissue. The protrusion is considerably less than immediately after surgery, causing only a gentle unevenness in the interior of the eye. The retina is reattached, slightly thinner than normal and shows some empty spaces (e) in the outer nuclear layer. (s) The sclera over the tube is about one half to one third thinner than originally.

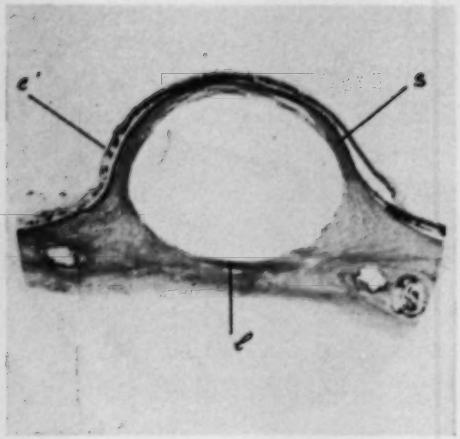

Fig. 15 (Dellaporta). (#11R) Operation area six months after surgery with the two-mm. tube. The latter is well enclosed between the sclera and the postoperatively formed collagen tissue. (t) Membranelike layer of flattened fibroblasts lining the tube; the retina is reattached, thinner than normal and shows some empty spaces (e) in the outer nuclear layer. (s) The sclera over the tube is about one-half thinner than originally.

24 to 48 hours after surgery, choroid and ciliary body being by that time three to five times thicker than normal; however, no infiltration by inflammatory cells occurs in the uvea. Thereafter, the inflammatory symptoms in the subchoroidal space and the hyperemia of the uvea subside quite abruptly so that four to five days after surgery they have essentially disappeared. These changes are most probably the direct result of the surgical trauma and were also observed after experimental lamellar scleral resection.[9,10]

In contrast, the swelling of the ciliary body amounting to 1.5 to 3.0 times its normal thickness together with markedly increased pigment, scattered and in clumps, persists for about four to five weeks after surgery. A similar swelling of the choroid, but without increased pigmentation, extending from the wound area up to the posterior pole of the eye persists for about two to three months after surgery. This late and long-persisting uveal swelling without histologically visible signs of inflammation might be most logically attributed to circulatory disturbances from the operation.

Retina. Immediately after surgery the retina shows numerous meridional folds on the sclerochoroidal protrusion and one to three larger equatorial folds behind the protrusion as well as some fine equatorial rippling (figs. 4 and 5). These folds obviously cause the retina to detach from the pigment epithelium so that a limited flat detachment is produced on and behind the protrusion. —The meridional folds are not recognizable histologically since the sections run in meridional direction.—The equatorial folds are well visible but are fewer and much smaller than similar folds found after experimental penetrating or lamellar scleral resection.[9,10,22]

About the fourth day after surgery a few of the equatorial folds flatten out and in their former position small empty spaces in the outer nuclear layer become visible (fig. 9). These empty spaces are formed through necrosis and subsequent absorption of the nuclei and represent mechanical damage caused by the sudden bending of the retina at the summit of the folds during the operation.[9,10,22] However, the majority of the folds remain essentially unchanged and are visible in the retina which in the meantime again approaches the choroid. In the next weeks the folds flatten slowly and the retina as a whole reattaches gradually to the pigment epithelium. Three to four months after surgery the retina is found reattached over and behind the sclerochoroidal protrusion; it appears slightly thinner than normal through a moderate rarefaction of its cells and shows usually one to three small empty spaces in the outer nuclear layer (figs. 14 and 15).

In the subretinal space, one to three days after surgery some albuminous fluid is found which in single instances is still detectable in traces 10 days after surgery. This fluid obviously derives from the inflamed choroid.

C. Complications

The increased intraocular pressure created after tightening the scleral sutures frequently caused the iris to prolapse through the relatively big paracentesis incision. This necessitated a peripheral iridectomy in 16 eyes, 13 of them being cases in which the two-mm. tube was used. In two cases a small vitreous bead appeared after the iridectomy and here the paracentesis wound was closed with a fine catgut suture.

In three eyes the sclera was perforated one to three times at the insertion of the sutures during the operation. Histologically some blood was found in the subretinal space in these eyes which absorbed two to three weeks later.

D. Abnormal response to the operation

The above-described histologic findings indicate that the majority of the eyes tolerated the operation well. At the end of the six-month follow-up the polyethylene tube surrounded by only small nests of granulation tissue is well encapsulated by the original and newly formed scleral tissue. The aim of the operation to produce a permanent or at least a long-lasting sclerochoroidal protrusion is achieved.

In contrast to this typical response six eyes (three animals) enucleated 15, 20, and 40 days after surgery showed the following: huge collections of leukocytes, representing a localized abscess, surrounded the tube and the neighboring sclera (figs. 16 and 17). Also, the sclera enveloping the tube showed a marked infiltration by leukocytes. As a result of the necrosis of the scleral tissue the silk sutures lost their hold on the tissue, the scleral wound opened and the sclera enveloping the tube flattened to a considerable degree. The choroid lying over the tube showed swelling and dense infiltration with leukocytes; the retina appeared normal.

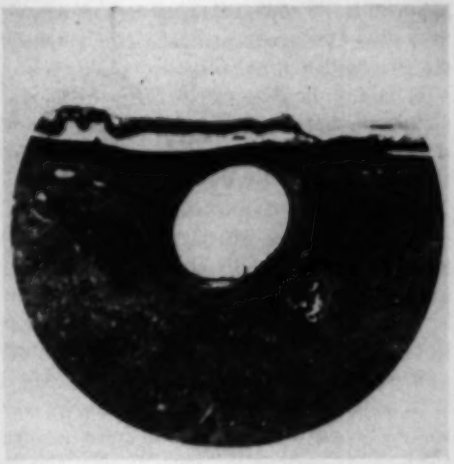

Fig. 16 (Dellaporta). (#18R) Abnormal tissue response to the tube 15 days after surgery. The sclera is flat. The tube is surrounded by dense leukocytic infiltration.

As far as can be judged from the small number of eyes involved the inflammatory signs and especially the leukocytic infiltration recede slowly leaving the sclera under the tube more or less flattened and the underlying choroid slightly fibrotic, with less

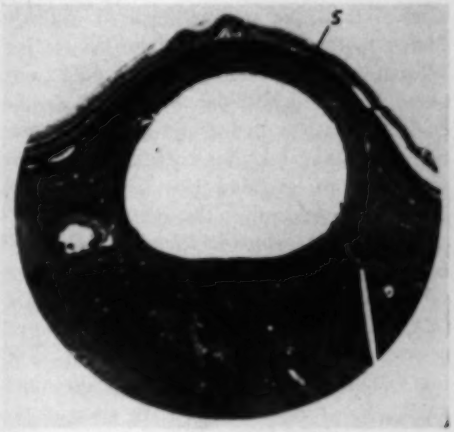

Fig. 17 (Dellaporta) (#18L) The left eye of the same animal shown in Figure 16. Identical dense leukocytic infiltration around the tube. (s) The sclera over the tube is also densely infiltrated by leukocytes.

pigment and firmly adhering to the sclera; the retina appears to reattach earlier than in the eyes with normal response.

It is my impression that the histologic picture of these six eyes represents a hypersensitivity of the respective animals to the foreign material of the polyethylene tube. This opinion is supported by the fact that always both eyes of the affected animals were involved, and to about the same degree. One can hardly consider the reaction as due to a common postoperative infection since in this case one would expect it much sooner after the operation.

It is obvious that such an abnormal response would jeopardize the intended results of the operation; even if the tube is not entirely extruded the wound will open and the sclera will be more or less flat again.

E. Effects of the operation

Comparison with related procedures

Effects of scleral resection operation. When the sclera is shortened by a penetrating scleral resection—or a lamellar scleral resection which has the same final effects—we know from previous experimental work[10] that the elastic choroid quickly adapts to the new space conditions so that one can consider sclera and choroid as one unit, the sclerochoroidal wall. Suppose we excise in such a hypothetical scleral resection operation (A) an equatorial strip of sclera 30 mm. long and three mm. wide. The operation would effect the following:

1. *The surface of the sclerochoroidal wall becomes smaller.* In our hypothetical case (A) the decrease of the surface of the sclera will be equal to the size of the excised scleral strip, that is, 30 mm. × 3 mm. = 90 mm.^{2}. The choroid follows closely the inner surface of the sclera, and its surface becomes smaller by the same amount. Therefore, a reattached retina in such an operated eye must cover a surface of choroid 90 mm.^{2} smaller than before the operation.

2. *Axial shortening of the eye.* If we should excise a 3-mm. wide circular scleral strip around the entire equator, the posterior pole of the eye will come to lie three mm. closer to the cornea, that is, the axial shortening will be three mm. If we excise a 30-mm. long and three-mm. wide equatorial strip, covering approximately one half of the equator, as in our hypothetical case (A), the axial shortening of the eye will be less than three mm. It is more accurate to express that effect by saying that, in the operated half of the eye, the surface distance between limbus and any point of the sclerochoroidal wall lying between the posterior wound lip of the excision and the posterior pole will be approximately three mm. shorter.

3. *The inner volume of the eye decreases.* The decrease corresponds to the shortening (90 mm.^{2}) of the surface of the sclerochoroidal wall.

Effects of scleral buckling operation. Suppose now that we perform a hypothetical scleral buckling operation (B) as described in this paper and enclose a polyethylene tube 30-mm. long and one mm. in the external diameter ($r = 0.5$ mm.). The strip of sclera which will envelop the tube after completion of the operation would be about 90 mm.^{2}. (Surface of cylinder $= 2\pi rh$, where r = radius of cylinder = 0.5 mm., h = length of cylinder = 30 mm.; that is $(2 \times 3.1416 \times 0.5) \times 30$ = about $3 \times 30 = 90$ mm.^{2}). This is the same size of scleral strip which we excised in our hypothetical case (A) of scleral resection. Our hypothetical scleral buckling operation (B) considered here will effect the following:

1. *The outer surface of the sclera becomes smaller,* but the inner surface area of the sclerochoroidal wall remains unaltered: In our hypothetical case (B) the scleral strip enveloping the tube is 90 mm.^{2}. This amount of sclera is pushed by the tube into the interior of the eye and is not any more a part of the external surface of the sclera which

is now smaller by 90 mm.². The sclera is pushed into the interior of the eye, producing a cylindrical protrusion, but since no sclera is excised, its inner surface area remains unaltered. The choroid follows closely the inner surface of the sclera over the protrusion. It is obvious that a reattached retina after such an operation will have to cover a surface of choroid equal to that existing before the operation.

In this point there is a fundamental difference between our two hypothetical operations. After the scleral resection (A), a reattached retina will have to cover a choroidal surface 90 mm.² smaller than before the operation, whereas after the scleral buckling (B), a reattached retina will have to cover a choroidal surface equal to that existing before the operation.

2. *Axial shortening of the eye.* If we should perform a circular scleral buckling operation, with a tube one mm. in diameter, around the entire equator, the posterior pole of the eye will come to lie three mm. closer to the cornea, that is the axial shortening will be three mm. If we perform the same buckling operation and enclose a tube 30-mm. long and one mm. in diameter, covering approximately one half of the equator, as in our hypothetical case (B), the axial shortening will be less than three mm. It is more accurate to express that effect by saying that in the operated half of the eye, the surface distance between limbus and any point of the sclerochoroidal wall lying between the posterior wound lip of the folding and the posterior pole will be roughly three mm. shorter.

Therefore, the axial shortening of the eye will be identical in both our hypothetical operations of scleral resection and scleral buckling.

3. *Decrease of the inner volume of the eye.* Its amount will be the addition of (a) the decrease of volume corresponding to the shortening of the outer surface of the sclera, which is identical to the decrease of volume in our hypothetical resection operation (A) and (b) a decrease of volume equal to the volume of the sclerochoroidal protrusion. The volume of the latter consists of the volume of the tube plus the enveloping sclerochoroidal wall.

Therefore, the decrease of the volume of the inner eye in the scleral buckling operation (B) will be considerably more than in the scleral resection operation (A).

4. *A cylindrically shaped protrusion of the sclerochoroidal wall* into the interior of the eye just behind the ora serrata covering approximately one half of the equator. Immediately after surgery, the protrusion will be one mm. high and one mm. wide plus the thickness of the sclera and choroid enveloping the tube.

In this point the scleral buckling operation differs fundamentally from the scleral resection in that it produces a permanent or at least a long-lasting protrusion of the sclerochoroidal wall, which in a case of retinal detachment will cause a cylindrically shaped area of choroid at the equator to come to lie nearer the detached retina.

In summarizing the effects of our two hypothetical operations, we might conclude that the *scleral resection operation* causes:

1. Decrease of the surface of the sclerochoroidal wall which has to be covered by a reattached retina.

2. Axial shortening of the eye.

3. Decrease of the inner volume of the eye.

The *scleral buckling operation* will cause:

1. *No* decrease of the inner surface of the choroid which has to be covered by a reattached retina.

2. Axial shortening of the eye identical to that in scleral resection.

3. Decrease of the inner volume of the eye considerably higher than that caused by the scleral resection.

4. Permanent or at least a long-lasting cylindrical protrusion of the sclerochoroidal wall into the eye.

According to experimental and clinical observations the shortening of the sclerochoroidal wall seems to be the decisive factor for the curative effects of the scleral resection in retinal detachment. The axial shortening of the eye being equal in both operations and since no shortening of the choroid occurs after scleral buckling, the curative factor of this operation can only be the protrusion of the sclerochoroidal wall into the eye. The considerable decrease of the volume capacity of the eye after scleral buckling causes a temporary increase of pressure on the membranes of the eye by the fluid contents. This does not seem to have any significant curative effect on a retinal detachment. The same effect can be produced by injecting normal saline solution into the vitreous cavity but this seems to be without result in the hands of most surgeons.

After experimental lamellar resection in normal dogs' eyes, retinal folds and an artificial retinal detachment were observed along the scleral excision. These retinal changes were attributed to the surplus retinal tissue created by the shortening of the sclerochoroidal wall.[9, 10]

The question arises why similar retinal folds appear also after experimental scleral buckling since according to the above conclusions the inner surface of the sclerochoroidal wall remains unaltered in area. The folds in this case are much fewer and much smaller than those observed after scleral resection. Their appearance might be explained by the slight decrease of the inner surface of the choroid from (a) the considerable thickening of this membrane extending from the protrusion up to the posterior pole of the eye and (b) the localized detachment of the choroid from the inner surface of the sclera at the posterior and occasionally the anterior foot of the protrusion (fig. 7-d).

A similar swelling of the choroid lasting for several days was observed behind the wound after experimental lamellar scleral resection.[9, 10] It was then explained that the choroid became thicker in order to compensate for its surplus tissue created by the shortening of the sclera. This explanation does not seem to be correct since a much more pronounced and much longer-lasting thickening of the choroid appears after scleral buckling operation where no choroidal surplus tissue is created.

The most logical explanation would be that both operations cause an edema of the choroid by impeding the venous outflow in the operated half of the eye. After lamellar scleral resection the choroid flattens soon after the operation and the normal outflow is re-established after several days; after scleral buckling, because of the permanent or long-lasting protrusion, the hindrance of outflow and the swelling of the choroid lasts for two to three months.

Summary and Conclusions

A scleral buckling operation with insertion of a polyethylene tube performed on normal dogs' eyes showed the following:

1. The operation produces a permanent or long-lasting cylindrically shaped protrusion of the sclerochoroidal wall and the retina into the interior of the eye.

In the eyes in which the one-mm. tube was inserted the height of the protrusion remains practically unchanged for six to eight weeks. Thereafter the protrusion is found to be one third to one half of the original height so that the final effect is a slight unevenness of the interior of the eye along the operated area.

In the eyes in which the two-mm. tube was inserted the height of the sclerochoroidal protrusion decreased only slightly during the six-month follow-up, the final protrusion being about 1.5 to 2.0 mm.

2. The surface area of the choroid is not altered by the operation.

3. The operation causes a considerable decrease of volume capacity of the eye.

4. Most of the animal eyes tolerated the

operation well, the tube having been finally encapsulated with but little tissue reaction. However, six eyes showed a late violent tissue reaction around the tube which is thought to be due to individual hypersensitivity to the polyethylene material, and which jeopardized the intended effects of the operation.

With regard to the pathology of the human eye the following conclusions may be drawn:

1. Performed on an eye with detached retina the scleral buckling operation would cause a cylindrical or spindle-shaped area of the choroid at the equator to come to lie closer to the separated retina.

2. After a scleral buckling operation the reattached retina will have to cover a surface area of choroid equal to that existing before the operation.

3. Since the human sclera is much thicker than that found in dogs the tendency of the sclera to unfold would be much stronger. It would therefore be advisable to perform a lamellar resection on the strip of sclera which has to envelop the tube. This procedure would also create real wound lips at the edges of the scleral folding which would heal more quickly and safely.

4. Considering that humans are more prone than animals to hypersensitivities, it is justifiable to assume that humans also might be sensitive to the polyethylene tube. In such cases the intended effects of the operation would not materialize and the surgeon might be confronted with a slow extrusion of the tube.

In view of these findings one would be justified to assume that a favorable clinical effect of the scleral buckling operation would be due to the sclerochoroidal protrusion which causes a band-shaped area of choroid to come closer to a detached retina. The long-lasting swelling of the choroid in the operated half of the eye might be an additional factor in bringing the choroid nearer to the detached retina.

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LEIOMYOMA OF THE CILIARY BODY*

Report of a case exhibiting a significant uptake of radioactive phosphorus

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For nearly a century there have been sporadic reports of leiomyomas occurring within the eye. The incidence of these smooth-muscle tumors in the uveal tract is, in fact, extremely rare, although they are quite prevalent in the alimentary tract and in the uterus. Of the early reports of leiomyomas of the iris and ciliary body, the authenticity of only a few is generally accepted. Many of the original cases are believed to have been unpigmented malignant melanomas.

With routine hematoxylin and eosin stain, this type of neoplasm should, in most instances, be easily recognized by (a) the compact structure of interlacing and closely packed bundles of elongated spindle-shaped cells; (b) the long oval nuclei which tend to arrange themselves in palisade formation; and (c) the granular eosinophilic cytoplasm of the cells. In addition to these histologic characteristics, Verhoeff demonstrated, in 1923, the presence of myoglial fibers by the use of Mallory's phosphotungstic-hematoxylin stain. These fibers can also be demonstrated by the use of the Masson trichrome stain or by the gold-impregnation method. It was by differential staining that Verhoeff was able to present the first proven case of leiomyoma of the iris.

Among the pertinent and recent reports may be mentioned that of Erdbrink and Harbert in which they review the original publications recording 19 cases of leiomyoma of the iris and, in addition, present a case of their own.

A critical evaluation of 10 reported cases of leiomyomas of the ciliary body was made by Blodi who failed to find conclusive evidence for such a diagnosis in a single case. This author reported, in 1950, the first authenticated case of leiomyoma of the ciliary body—a case in precise conformity with all the histologic requirements.

The Ophthalmic Pathologic Laboratory of the Eye and Ear Hospital of Pittsburgh, Pennsylvania, has processed a total of 1,500 globes. Intraocular neoplasms were found in 147, or 12 percent of these eyes. In this group there were four tumors of the ciliary body, three of which were malignant melanomas and one a leiomyoma.

An additional case, which fulfills the necessary histopathologic criteria of a leiomyoma of the ciliary body, is reported here together with the finding of a significantly increased uptake of radioactive phosphorus (P^{32}) by this neoplasm.

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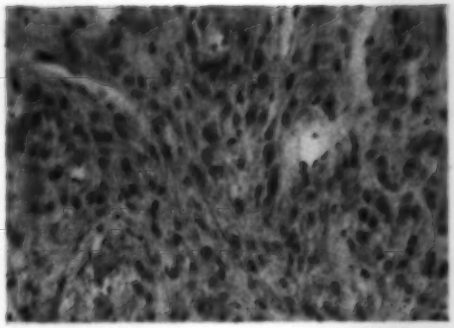

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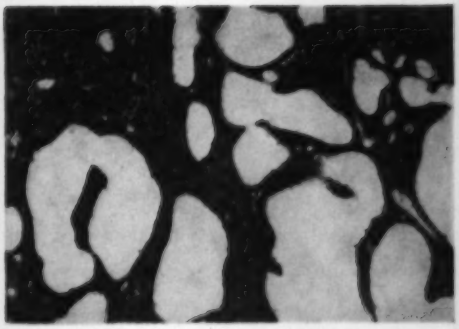

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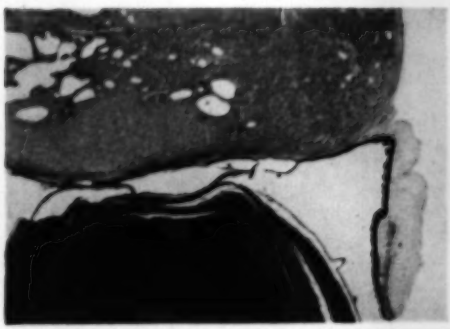

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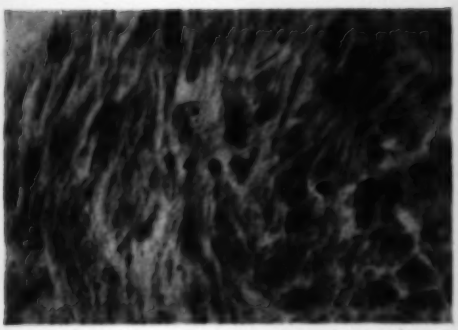

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Figs. 2-5 (Dunbar). Leiomyoma of the ciliary body.

Fig. 2. Leiomyoma of ciliary body showing interlacing muscle bundles. The cells have a spindle shape with a tendency toward pallisading of the nuclei. (Hematoxylin-eosin.)

Fig. 3. Unlined cystic spaces in tumor. (Hematoxylin-eosin.)

Fig. 4. Growth replacing root of iris and compressing lens periphery. (Masson trichrome stain.)

Fig. 5. Myofibrils in cytoplasm of tumor cells. (Masson trichrome stain.)

Case report

History. (D. M. Z. Unit number 13110. Service of Dr. G. R. Geeseman.) A 49-year-old white woman experienced a severe and sharp pain in the left eye while playing bridge. The pain was transient, lasting approximately one hour. There was no history of previous eye trouble. Following the disappearance of the pain, there was no complaint. The following day a slight and temporary blurring of vision in the left eye was noticed. The patient was examined by Dr. R. H. Davies two days after the original episode of pain. He found the visual acuity to be 20/30 in each eye without correction. The left eye revealed the presence of an iridodialysis located at the 12-o'clock position. This measured approximately 1.5 by 1.0 mm. There was an absence of cells in the anterior chamber and no hyphemia on slitlamp examination. The upward movement of the eye revealed a solid appearing mass which was clearly visible posterior to the area of iridodialysis. The mass also presented in the area of the iridodialysis.

Funduscopic examination revealed an absence of any retinal separation. Transillumination of light was nil in the area of the mass. No abnormalities were found in the right eye.

Except for the eye findings, the general physical examination was entirely negative. Blood pressure was 110/80 mg. Hg. The urinalysis, blood count, blood sugar, and blood nonprotein nitrogen did not exceed normal limits.

A radioacitve phosphorus (P^{32}) count was increased in the area of the neoplasm (fig. 1). Adjoining numbers in Figure 1 indicate a repeat count. Since the clinical diagnosis was malignant melanoma of the ciliary body, the eye was enucleated.

Pathologic report (E.E. 2030)

The eye was fixed in 10-percent formalin.

Macroscopic. The globe is firm and measures 26 by 24 by 23 mm. The cornea presents a diffuse haze (fixative solution.) The lens and iris are not seen clearly. The anterior chamber appears of normal depth. The globe was sectioned vertically. There is a pigmented neoplasm of the ciliary body which has flattened the equator of the lens at the upper pole. The lens remains in situ. No retinal separation is noted.

There appears to be slight cupping of the optic disc. The tumor measures 5.0 by 7.0 mm., and has a uniform dark brownish pigmentation on its surface. On sectioning, the neoplasm presents a uniform, whitish and solid appearance being pigmented only on its surface.

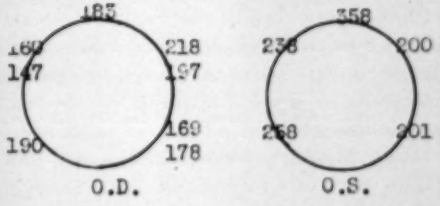

Fig. 1 (Dunbar). The radioactive phosphorus count was increased in the area of the neoplasm. Adjoining figures indicate a repeat count.

Microscopic. There is a large unencapsulated neoplasm replacing the entire ciliary body. The tumor is slightly larger than the crystalline lens. It has replaced the root of the iris and extends for a short distance into the anterior chamber. The tumor lies directly on the surface of the sclera and extends posteriorly to the region of the ora serrata. The inner surface is completely covered by the ciliary epithelium. It has compressed the lens periphery. The inner half of the neoplasm shows numerous cystic spaces which are empty. These spaces are separated by wide bands and at times a thin strand of tumor cells. There is no lining of the cyst spaces. The tumor is moderately vascular having occasional large sized vessels and many small capillaries.

The tumor is composed entirely of inter-

lacing muscle fibers. The muscle fibers are arranged in bundles some of which are cut longitudinally and others transversely. The cells have a spindle shape with long tapering fibrillar processes. The cell boundary is indistinct. The cytoplasm stains acidophilic. The majority of the nuclei vary from round to oval in shape and have a distinct nuclear membrane. In most instances a nucleolus is present and is associated with numerous fine and occasional coarse chromatin particles. Mitotic figures are inconspicuous. At many points there is a tendency toward pallisading of the nuclei. There is no intracellular or extracellular pigment deposits in the neoplastic tissue.

With Masson's trichrome stain the cytoplasm takes a characteristic dull lavender color. The stain demonstrates the presence of myofibrils without the formation of cross striations. The growth is composed entirely of intertwining muscle bundles and small blood vessels. There is a total absence of any stroma. The anterior surface of the growth extending into the anterior chamber is covered by a single layer of connective tissue cells.

The remaining structures of the globe are not remarkable.

Pathologic diagnosis. Leiomyoma of the ciliary body.

Discussion

This case is the first known instance of a positive radioactive phosphorus (P^{32}) count in a leiomyoma occurring in the eye. Erdbrink and Harbert were unable to demonstrate an increased P^{32} uptake in their case of leiomyoma of the iris. They concluded that the affinity of P^{32} for a neoplasm was a measure of its malignancy. But, when we consider the size (three mm.) and the location of the tumor in their case, it is not surprising that an increased count could not be obtained. Snodgrass, et al., were unable to demonstrate an increased uptake in their case of malignant melanoma of the iris (Case 4) in which the growth had extended to the posterior surface of the cornea. In this instance the Geiger counter was separated from the tumor only by the thickness of the cornea. In the case of Terner, et al., in which an increased P^{32} uptake is reported in a malignant melanoma of the iris, the reliability of the diagnosis cannot be accepted in the absence of histopathologic confirmation. It is interesting that in their series of 30 histologically proven malignant melanomas of the choroid, they report false-negative tests in 10 percent of the cases. Therefore, it is obvious that this test presents extremely doubtful results in small iris neoplasms while, in larger growths of the choroid and ciliary body, it has considerable value as supportive evidence in the diagnosis of neoplasm.

In reviewing the reports of this diagnostic procedure, it becomes apparent that certain variables influence its results; namely, (a) the accessibility of the tumor to the Geiger probe, (b) the vascularity of the neoplasm, (c) the metabolic activity of the tissue at the time of the test, and (d) other undetermined factors. The operation of unrecognized factors is evidenced by situations in which the test is negative but, on repetition, yields a positive result in cases where there are additional and irrefutable confirmatory data in the diagnosis of neoplasm (Case 100, Eisenberg, et al.). Despite these difficulties, P^{32} studies appear of definite value in the differentiation of neoplastic from nontumorous ocular disease. The test is of much less value in distinguishing malignant from nonmalignant growths.

Summary

An additional case of leiomyoma of the ciliary body is presented.

An increased radioactive phosphorus uptake by this neoplasm impairs the clinical value of the test in differentiating a leiomyoma from a malignant melanoma.

The differentiation of the histologically

benign leiomyoma from the malignant melanoma, which occurs with greater frequency and in the same location, is clinically important because of the obvious implications for the patient's life expectancy.

Eye and Ear Hospital (13).

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BENIGN MELANOMAS OF THE RETINAL PIGMENT EPITHELIUM*

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New York

Introduction

Out of a total of 151 eyes in which a fundus lesion raised the question of malignant melanoma of the choroid, nine eyes showed a singular finding which is our purpose to describe in this communication. It is our belief that these cases represent benign melanomas of the retinal pigment epithelium.

It is commonly accepted as a true paradox that the retinal pigment epithelium proliferates readily in response to noxious stimuli of an inflammatory nature but rarely, if ever, undergoes true neoplastic proliferation. Contrariwise, the choroidal, pigment-bearing cells do not reproduce their kind in response to stimuli, but they are a common source of benign or malignant melanomas. Consequently, any circumscribed pigmented area of the fundus which does not appear consistent with the usual sequelae of chorioretinitis is regarded by exclusion as a possible benign or malignant melanoma of the choroid.

We are confronted, therefore, with the problem of identifying and separating from choroidal tumors as many simulating lesions as possible. Our nine cases, of which seven are here described, were all viewed as suffi-

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ciently suspicious of malignant melanoma to warrant its serious consideration. However, their characteristics seem distinctive, and these we shall attempt to portray in this paper.

Clinical appearance

The lesion is unilateral, isolated, black, sharply demarcated, and flat. The shape is irregularly round or oval. The size is one to three disc diameters. The normal retinal vascular pattern courses undisturbed over the lesion. The pigmentation is uniformly black to gray except for occasional small unpigmented areas with sharp borders. These changes are placed in the pigment epithelium because of the black color, the sharp outline, and the clarity of the granular tissue markings. The pigment areas show no progressive changes. Field defects corresponding to the lesions cannot be elicited. The eyes harboring these pigment foci seem otherwise normal and comparable to the fellow eye. The involved eye shows no indication of an acquired pathologic process or foci elsewhere in the fundus, suggesting choroiditis. As far as we can say, there are no familial factors. There seems to be no correlation with general body pigment or pigmented lesions.

Cases

Case 1. (A. H.) A white woman, aged 42 years. A pigment area was discovered at routine eye examination and a question of a malignant melanoma of the choroid arose. The area was located in the midzone of the lower nasal quadrant of the left fundus. It was circular, two disc diameters in size, black, well circumscribed, slightly pale in the center, and with a granular appearance. The retinal vessels crossed the lesion undisturbed.

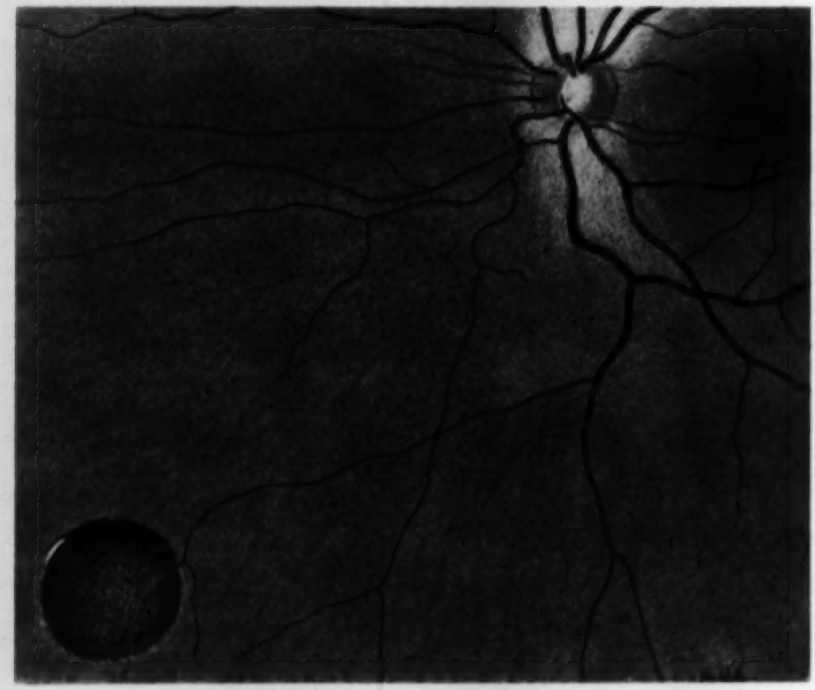

Fig. 1 (Reese and Jones). Case 1 (A. H.).

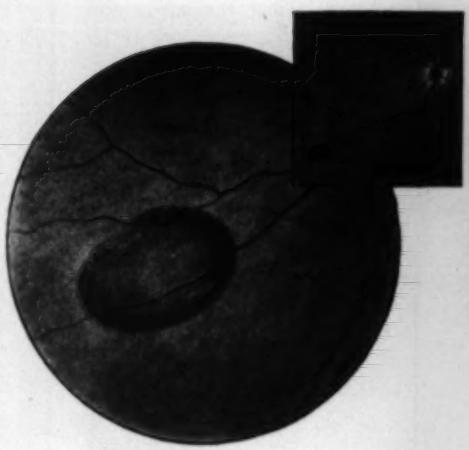

Fig. 2 (Reese and Jones). Case 2 (R. A.).

Case 2. (R. A.) A white girl, aged 17 years. A pigmented lesion was discovered in the fundus of the right eye at routine eye examination and the question of a malignant melanoma of the choroid was raised. It was located at the equator in the lower temporal quadrant, was oval, dark gray, and about two disc diameters in the long axis. There were several nonpigmented areas present, one breaking through the border. The retinal vessels crossed undisturbed.

Case 3. (S. T.) A white man, aged 54

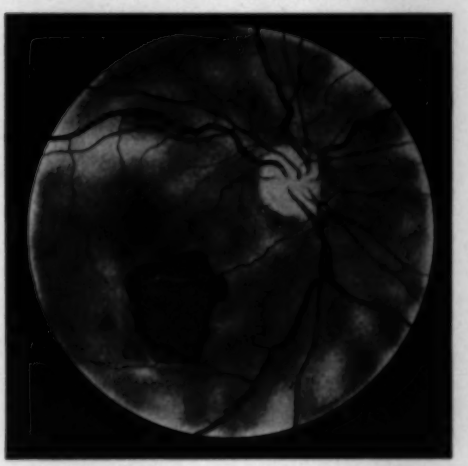

Fig. 3 (Reese and Jones). Case 3 (S. T.).

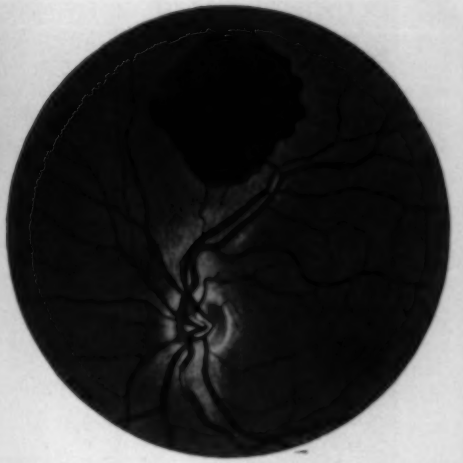

Fig. 4 (Reese and Jones). Case 4 (C. D.).

years. An area thought to be a melanoma was discovered during an examination for detached retina of the opposite eye. The lesion was located below the right macular area, was irregularly round, two disc diameters in size, and densely black with a granular-appearing surface.

Case 4. (C. D.) A white woman, aged 61 years. An irregularly square, dark-gray pigmented spot, three disc diameters in size, was discovered incidentally during a fundus examination. The borders were sharp and two nonpigmented lacunae broke through the border. Retinal vessels crossed undisturbed.

Case 5. (W. K.) A white man, aged 29 years, had a lesion in the left fundus thought suspicious of malignant melanoma. It was located adjacent to the temporal border of the disc, was rounded with a black granular appearance, and sharply demarcated. Several large, pinkish, nonpigmented islands were present in the lesion.

Case 6. (M. K.) A white man, aged 47 years, had a routine eye examination after bumping his head. A dark, sharply demarcated lesion of three disc diameters was found above in the right fundus. It contained a nonpigmented area along the in-

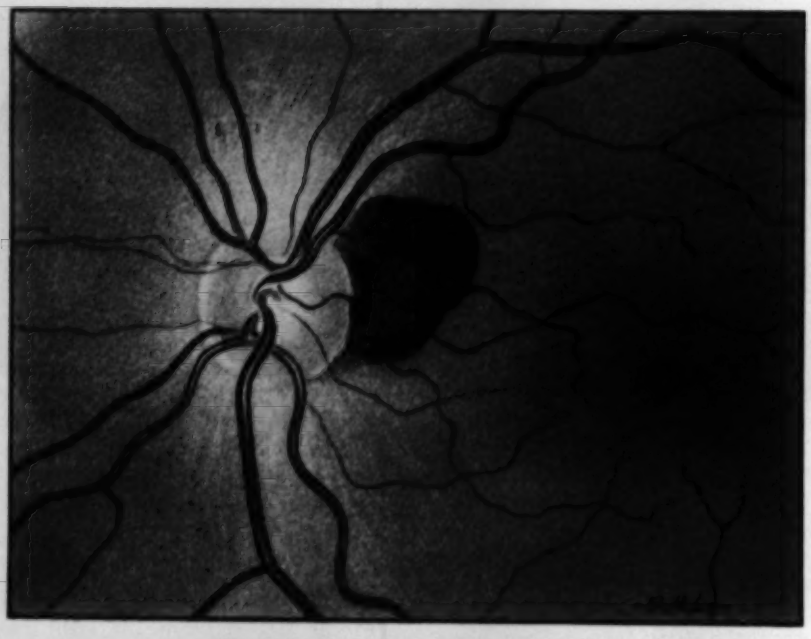

Fig. 5 (Reese and Jones). Case 5 (W. K.).

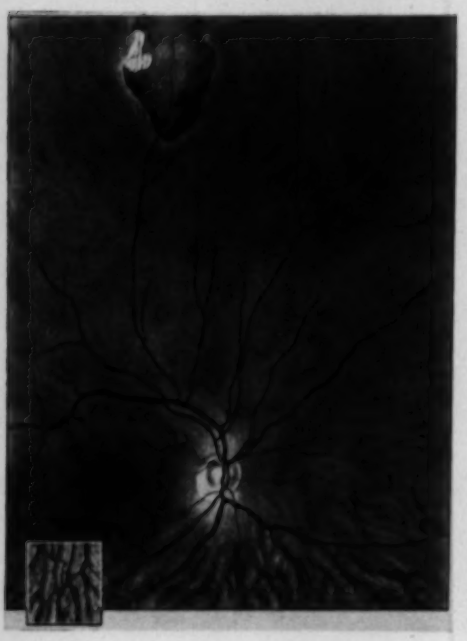

Fig. 6 (Reese and Jones). Case 6 (M. K.).

ferior border. No scotoma was found. Vision was normal.

Case 7. (D. C.) An adult female was found to have a two and one-half disc diameter, round, granular, dark area in the right eye along the inferior temporal vessels. It was not elevated, and the retinal vessels crossed it undisturbed. The patient saw many ophthalmologists whose opinions and interpretations varied. Because the possibility of a malignant melanoma still existed, the patient's apprehension mounted to the point where she requested an enucleation.

Pathology

Fortuitously, we have been furnished a drawing and a hematoxylin and eosin stained section from the patient described as Case 7. The section shows the pigmentation to be due essentially to excessive pigment epithelium. In the choroid under the site of the reduplicated epithelium, the melanoblasts are also more pigmented. They

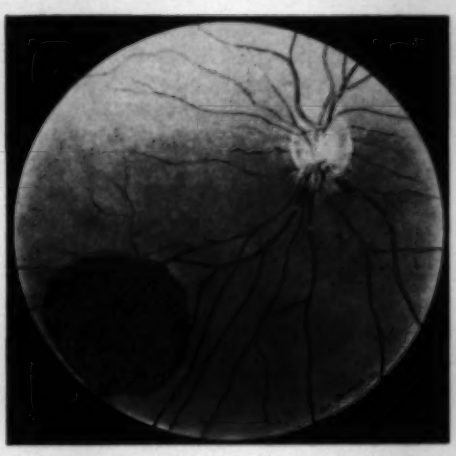

Fig. 7 (Reese and Jones). Case 7 (D. C.).

do not appear to be abnormal or excessive in number. The increased pigment content of these stromal melanoblasts does not seem to be from phagocytosis of pigment from the epithelium. There is no evidence at all of present or past inflammation or its sequelae. Our feeling is that this represents a localized, congenital overgrowth of pigment epithelium.

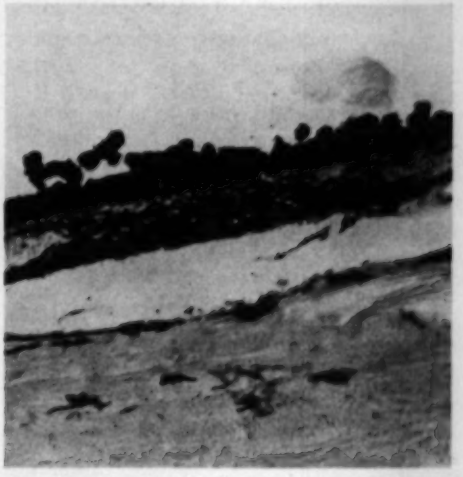

Fig. 8 (Reese and Jones). High-power section from Case 7 (D. C.).

Discussion

The isolated, sharply outlined black pigment area in the fundus described in this paper sometimes presents itself for differentiation from a malignant melanoma of the choroid. The black color, sharp demarcation, lack of elevation, and absence of a corresponding scotoma all bespeak against a melanoma of the choroid. We believe that serious consideration should be given the possibility that such pigment is a proliferative reaction from previous choroiditis. Our opinion is that such is not the case. Postinflammatory proliferation is not uniform but tends to be around the periphery or mottled. It shows progression following the active stage and most important is that in our cases there were no other foci in the fundus of the same or fellow eye. Furthermore, the section of the enucleated eye revealed no evidence or sequelae of inflammation. It is true that postinflammatory proliferation of the pigment epithelium can produce a fundus lesion which simulates closely the one which we are describing and no doubt could produce one rarely that might be indistinguishable. This would be possible when the noxious factor in the choroid was short of being lethal to the overlying epithelium, and, therefore, only stimulating, thus provoking the proliferation of a sheath of pigment epithelium. Under the usual conditions the noxious agent is lethal to the overlying epithelium and stimulating to the epithelium around the periphery of the inflammatory focus thus producing the usual postinflammatory fundus picture of a light center surrounded by a collar of pigment. Depending on the degree of toxicity, we may see all degrees of pigmentation from this usual picture to that of a lesion resembling the one we described here.

Whether or not this isolated congenital pigment area is related to the retinal pigment spots described as "bear tracks" or congenital group pigmentation of the retina is not clear. If so, we would expect some

cases to show transitions. In none of our cases did we see any accompanying lesions similar to "bear tracks." However, in Hoeg's extensive description of congenital grouped pigmentation of the retina, he described solitary lesions, in addition to the grouped spots, which answer the description of ours.

Pigment areas which appear to be similar to the ones we discussed have been described under various names and with various interpretations by Jaeger, Stephenson, Batten and Spicer, Dodd, Roll, Deutschmann, Segalowitz, and Crespi. These are the reports of isolated cases and in no instance has there been a concerted effort to assign the lesion a definite interpretation. We feel that the lesion is more common, definite, and consistent than the literature indicates and deserves the recognition of being an entity.

Conclusion

There is a type of benign melanoma of the pigment epithelium which is sometimes confused with a malignant melanoma of the choroid. The lesion is congenital and so far as we know it never becomes malignant.

73 East 71st Street (21).

We wish to express our appreciation to Dr. W. M. Boles and Dr. Stirling S. McNair for permission to use one case.

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STATISTICAL OBSERVATIONS OF ATOM-BOMB CATARACTS

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Yonagi City, Japan

Contrary to our expectation only a few cases of atom-bomb catract were experienced until 1952. There are, however, many patients suffering from radiation cataract among atom-bomb survivors to date. The cataract itself is so mild that the patients do not complain of any visual disturbance, even if they have characteristic yellow-golden glistening, round or oval or doughnutlike opacities at the posterior pole region of the lens. The atomic raid occurred in August, 1945, more than 10 years ago. We should like to present the statistical observations of Dr. Yoshiya Masuda, head of the Department of Ophthalmology, Red Cross Hospital, Hiroshima, Japan.

We should like to express our heartiest thanks to Ronald Atmore Cox, M.D., Professor of Ophthalmology, George Washington University, and Sidney John Glueck, M.D., Department of Ophthalmology, District of Columbia General Hospital, who assisted in preparation of this paper.

Statistical observations

1. *Incidence.* This consists of 435 patients examined from June 1, 1953, to October 31, 1954. Among them, 354 came directly to the eye clinic for examination and 81 were transferred from the other clinics, such as dermatology and surgery clinics. Of these, 116 patients (26.6 percent) were suffering from atom-bomb cataract, and 37 other cases were possibly of the same etiology.

In 1953, Dr. Hirose at Nagasaki University reported that 182 survivors (41.8 percent) showed cataract, and Dr. Shinsky[1] at Hiroshima in the same year said that, among 165 survivors, who experienced epilation, 135 cases (81.8 percent) were suffering from cataract.

2. *Age.* Among 113 patients under 15 years of age, 42 (37.2 percent) were suffering from radiation cataract; 16 to 25 years, 91 cases—23 cataract patients (25.2 percent); 26 to 40 years, 104 cases—26 cataract patients (25.0 percent); over 41 years, 127 cases—20 cataract patients (15.7 percent) (table 1). The greater percentage of cataracts were noted in the younger patients. The younger the tissue the more sensitive it is to radiation. The patients who are under 15 years of age received the atom-bomb injuries when they were under five years of age.

3. *Regarding visual acuity,* there were many cases with normal vision even though cataract was clinically visible. In 62 cases, 54.8 percent, vision was better than 20/20. Only four patients had vision under 20/200 (3.54 percent). Fifty patients had vision between 20/25 to 20/100 (44.2 percent). It was surprising that the cataract was so mild that, without careful examination by oblique illumination of the slitlamp, it could escape recognition (table 2).

4. *Clinical findings.* The opacity was mostly disclike but sometimes was doughnut-shaped or like a half doughnut, and, very rarely, irregularly shaped. These opacities were situated under the posterior capsule around the posterior pole region of the lens. The patients could not tell when these opacities occurred and did not notice even the slightest disturbance of the vision. It seems clear that these mild opacities become worse as time goes on and the patients will become blind sooner or later.

TABLE 1

PERCENTAGE OF RADIATION CATARACT ACCORDING TO AGE

Age (yr.)	Examined Cases	Cataract Cases	Rate (%)
Under 15	113	42	36.2
16–24	91	28	30.7
26–40	104	26	25.0
Over 41	127	20	15.7
Total	435	116	26.6

TABLE 2

VISUAL ACUITY OF PATIENTS WITH RADIATION CATARACT

Vision	Cataract Cases	Rate (%)
Over 20/20	62	53.5
20/25–20/200	50	43.1
Under 20/200	4	3.4
Total	116	100.0

Judging from a study of these cataracts, it would seem that many sufferers from the atom bomb, whose total doses exceeded the lethal dose, were deceased before cataract resulted from the radiation effect on the whole body. Survivors who now have or are going to develop atom-bomb cataract received less than lethal doses of radiation to the body. The dose to the eye was so small that cataract development has been insidious and the incubation time has extended over several years.

5. *Relation of cataract cases to distance from the zero ground of atom-bomb raid.* Of 159 cases whose distance from zero ground was under two kilometers, 87 (54.7 percent) were suffering from radiation; between two to three kilometers, among 123 cases were 25 cataract patients (20.3 percent); between three to four kilometers, among 26 cases, there were four cataract patients (15.4 percent); there were almost no cataract cases over four kilometers. Cataract incidence, therefore, is shown to depend upon the distance from the raid center. Lens damage varied inversely to the distance from the bomb explosion. No lens damage was noted if patients were more than four kilometers away (table 3).

6. *Location of the atom-bomb survivors.* The number of the survivors indoors during the raid was 277; 75 were suffering from radiation cataract. Those outdoors were 158;

TABLE 3

DISTANCE FROM ATOM-BOMB EXPLOSION

Distance (kilometers)	Examined Cases	Cataract Cases
Under 2	159	87
2–3	126	25
3–4	126	4
Over 4	25	1
Total	435	116

41 had cataracts. These figures show no difference—radiation cataract may occur at the same rate indoors or outdoors. It seems peculiar but it is statistically true, and I am unable to explain the reason.

The number of the cases sustaining burns was 90 of which 25 had cataract. There were 185 traumatic cases, 61 with cataract. Forty-one survivors sustained trauma and burns, 10 had cataract; 119 cases showed no wounds, with 20 cases of cataract. Trauma and burning were the main hazards of the atom-bomb raid.

7. *Sex.* There was no difference between the sexes. Dr. Masuda has already operated four patients with radiation cataracts who have recovered perfect vision.

8. *Latent period of atom-bomb cataract.* The latent period before the lens opacity becomes clinically evident varies considerably. It not only depends on the radiation dosage but also on the age of the patients and the distance from the bomb explosion. Peter[2] reported that, in general, the greater the dose and the younger the patients the shorter was the period of cataract formation. However, two to four years is the average period, with extremes of two months to over six years (Kandori,[3] Ascher,[4] and Milner[5]). In cataract patients among atomic-bomb survivors in Japan, the latent period varied from six months to two and one-half years as reported by Tamura, et al.[6] and Cogan, et al.[7] Naval and Air Force physicians and scientists[8] reported in April, 1953, that contrary to expectation, among atom-bomb survivors in Japan only a small percentage suffered from radiation cataract. In the same year, however, Prof. Hirose at Nagasaki University and Shinsky[1] in Hiroshima pointed out that there were many patients who were suffering from radiation cataract. These conflicting reports would seem to indicate that the latent period of atom-bomb cataract may extend from two and one-half months to several years, as does the latent period in other radiation cataracts.

SUMMARY

Among 435 atom-bomb survivors, there were 116 cases of radiation cataract. The highest percentage of cataracts was among the younger patients. Patients retained good vision in spite of the cataracts. Vision was normal in over 53.5 percent of cases. Slit-lamp examination showed mostly disc or dishlike opacities, with some doughnut or half-doughnut and, very rarely, irregular in shape, at the posterior pole of the lens.

Tottori University.

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PRESENTATION OF THE PORTRAIT TO SIR STEWART DUKE-ELDER

The new Council Chamber of the Royal College of Surgeons was the scene of a ceremony of world-wide interest to ophthalmologists when, on April 26, 1956, Sir Stewart Duke-Elder was presented with his portrait. Hundreds of British and Commonwealth ophthalmologists, and many of Sir Stewart's friends from abroad, had subscribed to the presentation which took place in the beautiful surroundings of the Council Chamber paneled with oak from a tree which was planted in the reign of Queen Elizabeth I. At the same time, Lady Duke-Elder and Sir Stewart were associated in a personal gift of two handsome antique silver candlesticks.

The portrait of Sir Stewart Duke-Elder painted by the distinguished artist, Ruskin Spear.

The presentation was held during the course of the annual meeting of the Ophthalmological Society of the United Kingdom and was witnessed by a large gathering. All present will remember the occasion which was characterized by the polished speeches of presentation made by Mr. Gayer Morgan, president of the Ophthalmological Society of the United Kingdom, and Dr. John Marshall, president of the Faculty of Ophthalmologists. Mr. Morgan said:

There are two reasons why a distinguished person should have his portrait painted.

One is that his features are so irresistible that artists flock round begging to be allowed to put them on canvas—the other is that his friends and colleagues realize that his character and attainments are so outstanding that they wish to accord him one of the highest honors they can think of.

Sir Stewart has probably done more for ophthalmology than anyone since Sir William Bowman. His industry has been astonishing, and he has never spared himself, but above all he has had for years a vision of what British Ophthalmology should be in the future, and he has seen it come true and our specialty flourish.

I am sure you will agree that no one has been such a popular or successful overseas ambassador in ophthalmology. I often think with some amusement of the first meeting of an artist with his sitter. The latter looking with some apprehension at the artist—the artist surveying the collection of bumps and hollows and wondering how he can possibly find the clue to the real man behind them. Sometimes the meeting is a failure, but often, and I am sure you will agree in this case, it is a success and produces what we all hoped for.

You see in this portrait the quick bright determined and yet humorous eyes—the evidence of the midnight oil burned in the production of that monumental work for which in part we are honoring him today. There is the mouth just about to say

something quite outrageous! How did the artist know about that characteristic feature which we all expect and enjoy so much.

In fact here is Sir Stewart and I would like to congratulate artist and sitter on the production of something we shall all enjoy. We are happy also that we can associate this presentation with Lady Duke-Elder as she and Sir Stewart have chosen two silver candlesticks as a personal present from us all.

I will now pass you over to Dr. John Marshall, president of the Faculty of Ophthalmologists.

Dr. John Marshall said:

I count it a signal honor that as president of the Faculty of Ophthalmologists I have the privilege of assisting my fellow president of the Ophthalmological Society of the United Kingdom in this presentation to Sir Stewart Duke-Elder.

As a fellow Scot I feel that it would be appropriate to misquote the words addressed to John Shand in J. M. Barrie's play "What Every Woman Knows," words which might well have been addressed to the youthful Elder ere he left the kingdom of Fife—"A young man of your ability, let loose upon the world what could he not do? It's almost appalling to think of; especially if he went among the English." It is to take notice of this foray among the English that we are here tonight.

While we of the Faculty of Ophthalmologists are particularly indebted to him for his services in the medicopolitical and administrative fields of ophthalmology and to him as one of the founders, these are probably the spheres in which he himself would take least credit. It is to do honor to him for his work in completing a world textbook in ophthalmology—a book unique both in its completeness and its readability—a task of the magnitude of that of the seven maids with seven props which he completed in a mere 25 years while taking in his stride the administration of ophthalmology for the British Army, the duties of president of an International Congress and of president of the International Council of Ophthalmology, the editing of the *British Journal of Ophthalmology*, and above all the creation and control of the Institute of Ophthalmology.

Ophthalmology, national and international, owes an incalculable debt to this man of genius who with all his success and all his brilliance has still not had success go to his head. He has remained a leader—doubtless a successful strategist but never a dictator.

The factors responsible for this humanity are his charm which we have all experienced.

Secondly, his ability to meet men on their own level, to judge their abilities and to direct their energies to work for him on projects suited to those abilities and above all to see that they got the credit for that work.

He has a tenacity of purpose which has not allowed material success to cause any slackening of his efforts, he has enjoyed the fruits of success —material and academic—with a verve which has left younger men exhausted and yet produced a new volume at about the appointed day.

And finally, like John Shand in the play, he has been fortunate in his wife. I am sure that but for her he would not have been half the man that he is. How she has controlled and guided this man of genius I do not know but I do know that she has done what no body of men has ever succeeded in doing. We in ophthalmology owe to her almost as much as we do to her distinguished husband.

Sir Stewart is still a young man. We have in the Glasgow Eye Infirmary two portraits of William Mackenzie. In the first he is clean shaven, in the second he has a beard. I hope that 20 or 30 years hence some of the young men here today will have the privilege of presenting the bearded Duke-Elder with his second portrait.

Sir Stewart gave an endearing reply of acceptance of the portrait and gift, on behalf of himself and his wife, Phyllis:

What has been said about me and what has been given to me leaves me speechless with embarrassment. It cannot be true; it surely must be a dream; but at the same time I suppose Gayer Morgan and John Marshall are relatively critical and responsible people; and so I suppose there is something in it.

"How did all this happen?" I ask myself. I think I can best tell you by a parable. The parable deals with a young man who picked up a lady in Piccadilly. When he got to her flat he saw on one side of the bedroom a very large bookcase and, going up to it, he found that it was full of Latin and Greek texts. On the other side of the room he saw a similar bookcase and, on inspecting it, he found that it was full of advanced books on law. "How come?" said he. "Well," she said, "I studied classics at Oxford and then read law in the Middle Temple." "Then how did you take up a life like this?" "Oh," she said "just sheer good luck."

My luck has been largely in the people I have met and who have helped me. There was first of all Herring, my professor of physiology at St. Andrews. Then Sir John Parsons, who guided my young footsteps in ophthalmology at Moorfields and who introduced me to Sir Walter Fletcher at the Medical Research Council, and who told Phyllis that she had to marry me. There was also Bayliss and Starling at University College who inspired me in research and taught me its techniques. And, above all, there was Phyllis who has looked after me with great care for 28 years and who, in the early days, worked all day in the laboratory and most of the night in the study.

This, of course, is the way of the world. It is one task after another; but all great fun, all most enjoyable, and all a great adventure because each one leads on to another adventure.

You organize ophthalmology in the Army in the war and that leads to its organization in peace—from the medicopolitical point of view that means

starting the Faculty and taking an interest in the International Council; from the academic point of view it means starting the Institute of Ophthalmology. At the Institute before one year is over you are thinking of the budget for the next; and before one research project is finished you are planning the next two or three that it has suggested. You write one volume of a textbook and that leads to seven; and when the seventh is finished you turn to your desk and find a great pile of letters, all of them asking—some of them petulantly—why you have not written the first one over again; and so you start.

And so life goes on. I suppose it will all stop some time; but meantime an experience like this pulls one up with a jolt. Suddenly everything has changed; the objective has become subjective; facts have been overlaid with emotion.

It is not so much that you, forgetting my many faults and failures, have collectedly concluded that, on the whole, the things I have done have been good; it is the way that you have said so; it is your kindliness in telling me of it by this delightful ceremony and with this gift and the spirit it conveys.

It has been said that the gifts that we give each other in life are for the most part cold and expressionless because they convey so little of ourselves. The farmer should give of his corn, the sailor coral and shells, and the craftsman the product of his hands. Most things one gets in life—honors, position, and so on—are indeed cold and expressionless, and one leaves them behind with the other bits of tinsel that one gathers in life. But this will remain with me forever because of its emotional content; it is not cold and expressionless but warm and comforting. It is the type of thing that gives an entirely new aspect to life, that gives it a new meaning that one never suspected before. It is like falling in love with a woman or seeing a vision on the road to Damascus. It completely transforms life, which is never quite the same again.

For giving me this experience I give you my grateful thanks. From now on life for me will be less of a factual routine and more of a spiritual thing; because of this that you have done to me I will travel on with less of urgency and more of peace.

I only wish, looking at things from my subjective point of view, that I felt within myself that I were more worthy of the spirit of the gift. I only wish that I had done for opthalmology—and for you—as much as ophthalmology—and you—have done for me.

TOXOPLASMIC UVEITIS

Treatment with pyrimethamine and sulfadiazine

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Background

In 1938 and 1939, Wolf and Cowan[1] and Wolf, Cowan, and Paige[2] reported cases of natal or intrauterine chorioretinitis caused by Toxoplasma. Later articles by ophthalmologists[3,4] stressed the importance of Toxoplasma in congenital chorioretinitis. Prior to 1949, there was considerable speculation and scattered reports of adult chorioretinitis on a possible toxoplasmic etiology.[5,6] These speculations were dampened, however, by Walsh,[7] Hogan,[8] and Sabin[9] who concluded in a symposium on toxoplasmosis at the American Academy of Ophthalmology in 1949 that "there is no evidence that noncongenital acute chorioretinitis is caused by Toxoplasma." There the matter remained until the monumental report of Wilder[10,11] of the presence of "organisms morphologically indistinguishable from Toxoplasma," in the necrotic retina of 53 eyes of adults with chorioretinitis.

Woods, Jacobs, Wood, and Cook[12] studied the role of toxoplasmosis in adult chorioretinitis in a paper at the American Academy of Ophthalmology in 1953. Woods had had the foresight to preserve in the deep freeze

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the sera of many of his granulomatous uveitis cases since 1949. Their conclusions, based on a review of the charts and on Sabin dye tests on the preserved sera, were that Toxoplasma was a probable etiology in approximately 25 percent of the cases of adult granulomatous uveitis. A follow-up analysis on a later group of patients confirmed these findings with an even higher percentage of probable toxoplasmic etiology (44 percent).[13]

Jacobs, Fair, and Bickerton[14] established the final proof of the toxoplasmic etiology of adult chorioretinitis when they removed an adult eye with presumed toxoplasmic chorioretinitis and successfully cultured the Toxoplasma organisms on chick embryos and transmitted them in animal inoculation experiments.

Although the toxoplasmic etiology of adult chorioretinitis is well established, there is no agreement on the criteria for this diagnosis in an individual case. Besides the clinical evaluation of the patient and the careful attempt to rule out other granulomas as an etiology, there are two tests with positive significance, the Sabin dye test and the Toxoplasma skin test.

For the Sabin dye test, Beverly and Beattie[15] proposed as significant varying titers depending upon the age group:

Age (in yr.)	Positive titer
Below 10	1:8 or over
10-19	1:32 or over
Over 20	1:64 or over

Woods, et al.,[12] in general accepted these criteria. They also emphasized the importance of rising titers during the acute phase of the disease, as well as the clinical evaluation of the patient. Hogan[16] has perhaps been the most conservative of all in his statement that "unless the titers are 1:1,024 or more or show a fourfold increase, one is not justified in making a presumptive diagnosis of toxoplasmic chorioretinitis."

Jacobs, Cook, and Wilder[17] were able to obtain sera on 21 patients in whose eyes Wilder[11] had found Toxoplasmalike organisms. All of these patients had positive Sabin dye tests. However, only three had titers greater than 1:64 and three had titers of less than 1:16. They point out that, although in a random sampling of the general population, one might expect positive titers in 40 to 50 percent, the probability of positive titers in 21 out of 21 cases is one chance in 2,000,000. They emphasize that the only important finding is a positive dye test and that the titers on one determination alone are not significant. They further postulate that the reason for low titers in some cases of active chorioretinitis is that the organisms are confined to the uveal tract and consequently provide little antigenic stimulation.

In the case in which Jacobs, Fair, and Bickerton[14] were able to provide the final proof of the toxoplasmic etiology of adult chorioretinitis by culturing and transmitting the organism, the titer at the time of enucleation was only 1:64. Besides the lack of agreement on the significance of varying titers to the dye test, the picture for the average ophthalmologist is further complicated by the difficulty (and the length of time) in getting initial and serial dye test determinations.

There is likewise lack of agreement as to the role and the importance of the toxoplasmin skin test in the attempt to determine the etiology of adult chorioretinitis. Hogan[16] says that skin tests "are of value only for population surveys, and provide little evidence as to the causation of an individual case of uveitis." He makes this statement because skin tests provide no information on dye test titers and because some patients have negative skin tests and positive dye tests. However, if we accept the premise of Jacobs, et al.,[17] that it is not the level of the titer but the fact of a negative or positive dye test (in any dilution) which is most significant, then the toxoplasmin skin test assumes a much more important role.

Hoover, Naquin, Jacobs, Gans, Woods, and Wood[13] found some patients with nega-

tive skin tests and positive dye tests. They also found some with positive skin tests and negative dye tests—which they were unable to explain except by inaccuracies or nonspecificity of one or both of the tests.

Ryan, Hart, Culligan, Gunkel, Jacobs, and Cook,[18] in a report of 37 cases of presumptive toxoplasmic chorioretinitis, found that all had positive dye tests and 80 percent had positive skin tests. There were no cases of positive skin tests with negative dye tests. They suggest that because of the difficulty in obtaining them, dye tests might be reserved for the diagnosis of those cases with negative skin tests.

Results of treatment

Sabin[9] in the symposium on toxoplasmosis in 1949 discussed the treatment by saying that the sulfonamides were the only drugs at that time which had been shown to have a therapeutic effect in experimental animals. He felt that there was no justification for the use of sulfonamides in adult chorioretinitis because "the existence of noncongenital acute toxoplasmic chorioretinitis still has to be demonstrated."

Eyles[19] in 1953, on the basis of work on experimental animals, recommended sulfadiazine and pyrimethamine (2,4-diamino-5-p-chlorophenyl-6-ethyl pyrimidine, manufactured under the trade name of Daraprim®). Eyles also said, in his discussion on the paper of Ryan; et al.,[18] that the two drugs together are more than six times as active as would be expected from their additive action alone.

Ryan, Hart, Culligan, Gunkel, Jacobs, and Cook[18] reported on the treatment of 29 cases of presumptive toxoplasmic chorioretinitis with Daraprim® and sulfadiazine. Twenty-five of these cases (86 percent) showed a clinical response; eight cases (27 percent) showed improvement within seven days. Among their criteria for improvement were: (1) Ophthalmoscopic evidence of healing of the lesion; (2) clearing of the vitreous opacities; (3) improved visual acuity; (4) diminished flare and cells and resolution of the keratic precipitates.

Cassady, Culbertson, and Bahler[20] treated 11 cases of presumptive ocular toxoplasmosis with Daraprim,® sulfadiazine, and hydrocortisone. Of these cases, five showed marked improvement within one week, one marked and three moderate improvement at the conclusion of treatment.

Hoover, Naquin, Jacobs, Gans, Woods, and Wood[13] treated a series of cases with Daraprim® and sulfadiazine. Over half of them were improved.

Hogan[16] treated a series of suspected Toxoplasma patients with Daraprim® and sulfadiazine and felt there was no significant improvement. He did say, however, in the same article that "if the uveitis survey was negative for other causes, and if he felt the patient possibly had the chorioretinal lesions of toxoplasmosis he would treat him with Daraprim and sulfadiazine."

Treatment

Most of the reports on the use of Daraprim® and sulfadiazine have not used a fixed dosage. They have tended to individualize their dosage schedule and to change the length of treatment depending on the response and complications.

Ryan, et al.,[18] began by using 25 mg. of Daraprim,® three times daily, 0.5 to 2.0 gm. of sulfadiazine daily for 10 days. Later in their study, they lengthened the period of treatment (with lower dosages in the latter phases of treatment).

Cassady, et al.,[20] used 25 mg. of Daraprim®/60 lb. body weight and 1.0 gm. of sulfadiazine/60 lb. body weight for 10 days. The dosage was then cut in half and continued for about one month. They also used 20 mg. of hydrocortisone, four times daily, with the Daraprim® and sulfadiazine.

Frenkel in his discussion on the paper of Ryan, et al.,[18] suggested that although cortisone alone sometimes made the chorioretinitis from toxoplasmosis worse, in eyes under treatment with Daraprim® and sulfadiazine,

it should theoretically minimize the inflammatory reaction produced by the rupture of the pseudocysts.

Naquin, in reading the paper of Hoover et al.,[13] said that they used 25 mg. of Daraprim® every day for three weeks, then 25 mg. every other day for three weeks. Two gm. of sulfadiazine were given daily for the six-week period.

Toxic reactions from the drugs

All the reports have emphasized the necessity of adequate supervision of the patients undergoing treatment with these drugs and the dangers from their possible side effects. Although there have been no fatalities reported, both drugs are known to be in some cases depressants of the hematopoetic system.

Ryan[18] lists among the toxic manifestations which he encountered: (1) Nausea, anorexia, and weight loss; (2) depression of the formed elements of the blood; (3) rash. The rash responded to antihistaminics and in no case did depression of the formed elements fail to recover rapidly after cessation of the therapy or reduction to a level of 25 mg. of Daraprim®/day.

Cassady, et al.,[20] had one patient with severe depression of the white blood cell and platelet count necessitating discontinuation of the therapy and the administration of intravenous corticotropin.

Naquin[13] mentioned two cases of severe agranulocytosis requiring multiple transfusions.

Ryan says that there is suggestive evidence that younger patients tolerate the drugs better.

Material for this study

At the U. S. Naval Hospital, San Diego, California, from July, 1953, to December, 1955, there were 117 cases of uveitis whose records were available for review. The actual number of cases is considerably higher than this because most of the veterans' and dependents' charts were not available and because there is no system of filing under the diagnosis on patients who were not admitted, that is, who were treated solely in the out-patient clinic.

Out of the 117 cases, there were 69 who were classified as nongranulomatous and 48 as granulomatous. Of the granulomas, 12 had manifestations limited to the anterior segment (iridocyclitis) and 36 were generalized uveitis or limited to the posterior segment.

The uveitis survey which was done on many of these patients included:

I. General history and physical
II. Complete eye examination
III. Blood
  a. Hemoglobin
  b. White blood count and differential
  c. Sedimentation rate
  d. Agglutination for Brucella
  e. Kahn
  f. Fasting blood sugar
  g. Total serum protein and AG ratio
  h. Sabin dye test
IV. Urinalysis
V. X-ray
  a. Chest
  b. Sinuses
  c. Phalanges
VI. Skin tests
  a. PPD (first, intermediate and second strength)
  b. Histoplasmin
  c. Toxoplasmin
  d. Coccidiodin
  e. Brucellergin
  f. Frei
  g. Bacteria
    1. Beta hemolytic streptococci Group A (strains 1-10)
    2. Beta hemolytic streptococci Group A (strains 11-20)
    3. Beta hemolytic streptococci Group A (strains 21-30)
    4. Beta hemolytic streptococci Group A (strains 31-40)
    5. Beta hemolytic streptococci, Group B
    6. Beta hemolytic streptococci, Group C
    7. Beta hemolytic streptococci, Group D
    8. Beta hemolytic streptococci, Group F
    9. Beta hemolytic streptococci, Group G
    10. Alpha hemolytic streptococci
    11. Gamma hemolytic streptococci
    12. Staphylococcus toxin
    13. Staphylococcus aureus, hemolytic
    14. Pneumococcus, type 1
    15. Pneumococcus, type 2
    16. Pneumococcus, type 3

VII. Consultations
- a. Ear, Nose and Throat
- b. Genito-urinary
- c. Dental (including full mouth X rays)
- d. Others (if indicated from history and physical)

Not all of the 48 granulomatous cases had complete surveys, but of the 37 who did there were 15 cases whose surveys were negative except for a positive skin test to toxoplasmin (and where done a positive Sabin dye test).

Beginning in February, 1955, a series of nine patients with active uveitis have been treated with Daraprim® and sulfadiazine. On the basis of Frenkel's suggestion[18] several of them were given systemic cortisone as well.

All of these patients had careful histories, physicals, and ocular examinations. All of them had positive skin tests to toxoplasmin and all of them had uveitis surveys which were negative for other evidence of granulomatous etiology. In one patient (Case 7) although the only positive finding on the survey was a positive skin test to toxoplasmin, the history and ocular examination were more suggestive of another etiology than toxoplasmosis.

In none of these patients were serial dye tests available and in none were the results of the dye test available before treatment was begun. Sera were drawn on these patients before the institution of therapy and through the courtesy of Dr. M. J. Hogan and the Proctor Foundation in San Francisco, the results became available later. Where available, the results of the dye tests are listed in the case reports. All the cases in which the dye tests were done were positive.

Most of these patients were hospitalized for treatment. All of them were watched carefully for toxic reaction to the drugs. Complete hemograms were done either every day or every other day during the intensive phase of therapy. There were no cases with depression of the formed elements of the blood. There was one case with urticaria presumably due to the drugs. However, this was controlled with antihistaminics, allowing continuation of the therapy. The only other complications were slight anorexia and nausea. All of the patients were in the younger age group, the ages ranging from 12 to 27 years.

Report of cases

Case 1

History. R. E. S., a 27-year-old white man was admitted to the U. S. Naval Hospital, San Diego, California, on February 1, 1955. He said that his left eye had been red and the vision had been blurred about two days. He had no pain. He had had a chorioditis in the left eye in 1945 for which no cause had been found. There was no history of granulomatous disease.

Ocular examination. Visual acuity was 20/20 in the right eye and 20/80 in the left. The right eye was normal to slitlamp examination. Ophthalmoscopic examination of the right eye revealed a healed heavily pigmented area of chorioretinitis above the macula. There was moderate deep injection of the left eye and plus-two flare and cells. There were no synechia or keratic precipitates. There were moderate vitreous opacities in the left eye and there was a healed lesion above the macula similar to the one in the right eye. There was also a fresh lesion between this and the disc. This fresh lesion surrounded the superior temporal vessels as they came off the disc. The intraocular pressure was 23 mm. Hg in the right eye and 58 mm. Hg in the left (Schiøtz).

Uveitis survey. The following were normal or negative: CBC, Kahn, urinalysis, fasting blood sugar, agglutinations for Brucella, and total serum proteins and A/G ratio. The chest X-ray films revealed a healed primary focus. Skin tests to coccidiodin and PPD in all dilutions were negative. There was a 10 by 10 mm. reaction both to histoplasmin and to toxoplasmin. Sabin dye test (reported later) was 1:64.

In addition to local therapy, he was started on Diamox and fever therapy. On February 2nd his tension was 24 mm. Hg and on February 4th, 17 mm. Hg.

On February 10th, the vision was 20/60 and the intraocular pressure was 17 mm. Hg (reduction of the Diamox had already been started). The eye looked about the same. There was two-plus cells and flare and a few greasy keratic precipitates were present. He was started on Daraprim® 25 mg., twice daily and sulfadiazine (0.5 gm., four times daily).

On February 14th, the vision was 20/50 and there was no injection. He was started on cortisone 25 mg. four times daily.

On February 16th, the vision was 20/40. The keratic precipitates were less and the vitreous

seemed clearer. The Daraprim® was cut to 25 mg. every day.

On February 23rd, the vision was 20/30. There was only a plus one flare and no keratic precipitates. The vitreous was definitely clearer and the lesion seemed less "fresh." The Daraprim® was cut to 25 mg. every other day and the sulfadiazine to 0.5 gm., twice daily.

On February 28th, the vision was 20/25. The Daraprim® was cut to 25 mg. every third day and the cortisone to 25 mg., three times a day.

On March 5th, the cortisone was cut to 25 mg., twice daily.

On March 11th, the vision was 20/20. There was only a plus or minus flare and the vitreous was much clearer.

On March 26th, the vision was 20/20. There was no flare and there were no vitreous opacities. The chorioretinal lesion was still elevated but was less fresh in appearance and there was slight beginning pigmentation. The Daraprim® was cut to 25 mg. every week, the sulfadiazine was discontinued and the systemic cortisone was gradually discontinued. The patient was returned to light duty.

On May 31st, he was discharged to full duty (still on 25 mg. of Daraprim® every week) and followed in the eye clinic as an out-patient.

Although he was asymptomatic, ophthalmoscopically the lesion continued to have a slight "soft" appearance and he was continued on 25 mg. of Daraprim® weekly. On October 29, 1955, the lesion appeared completely healed. The visual acuity was 20/20. The vitreous and anterior chamber were clear. The Daraprim® was discontinued on this date.

CASE 2

History. A. E. S., a 22-year-old white man, was admitted to the U. S. Naval Hospital, San Diego, California, on December 27, 1954. He said that the vision in his right eye had been blurred for the past three days. There was no history of previous eye disease or injury.

Ocular examination. The visual acuity was 20/200 in the right eye unimproved with pinhole or lens and 20/20 in the left eye. There were many mutton-fat keratic precipitates in the right eye, plus-three flare and cells and heavy vitreous opacities. The fundus details were not clearly seen because of the opacities in the media. There was visible a fresh exudative lesion in the inferior nasal quadrant. The left eye was normal to slitlamp and ophthalmoscopic examination. The intraocular pressure was normal in both eyes.

Uveitis survey. The following were normal or negative: CBC, Kahn, urinalysis, fasting blood sugar, agglutinations for Brucella and total serum proteins and A/G ratio. X-ray films of the chest were normal. Skin tests to coccidiodin and PPD in all dilutions were negative. There was a 18 by 18 mm. reaction to histoplasmin and a 12 by 10 mm. reaction to toxoplasmin. Sabin dye test (reported later) was 1:64.

In addition to local treatment to his eye, he was given systemic penicillin and streptomycin and 100 mg. of cortisone daily. On February 21, 1955, visual acuity of the right eye was still 20/200 and the condition of the eye was essentially the same. He was started on Daraprim® 25 mg., twice daily, and sulfadiazine (0.5 gm., twice daily).

On February 28th, the Daraprim® was cut to 25 mg. every day and the sulfadiazine to 0.5 gm. every day.

On March 4th, the Daraprim® was reduced to 25 mg. every other day and the sulfadiazine to 0.5 gm. every other day.

On March 16th, the keratic precipitates were largely resolved. There was only a plus or minus aqueous flare. The vitreous opacities were less and the visual acuity was 20/50.

On March 23rd, the visual acuity was 20/40. There was no reaction in the anterior chamber. The vitreous opacities were clearing.

On March 25th, the Daraprim® was cut to 25 mg. three times a week and the sulfadiazine to 0.5 gm. three times a week.

On June 7th, the vision was 20/20 — 2. There were still slight opacities in the vitreous but the eye was otherwise quiet and the lesion was well pigmented.

On June 20th, he was discharged.

CASE 3

History. J. R. M., a 23-year-old white man, was admitted to the U. S. Naval Hospital, San Diego, California, on January 21, 1955. He said that the vision had been poor in his left eye for many years. He had been previously hospitalized for recurrent attacks of uveitis with little improvement.

Ocular examination. The visual acuity was 20/20 in the right eye and 20/100 in the left eye unimproved with lens or pinhole. There was moderate circumcorneal injection of the left eye and a plus-two flare and cells. There were no synechia or keratic precipitates. Marked vitreous opacities obscured fundus details. There was visible an exudative lesion in the inferior temporal quadrant. The right eye was normal to slitlamp and ophthalmoscopic examination. The intraocular pressure was normal in both eyes.

Uveitis survey. The following were normal or negative: CBC, Kahn, fasting blood sugar, agglutinations for Brucella, and total serum proteins and A/G ratio. The chest X-ray film was negative. Skin test to histoplasmin, coccidiodin, Brucellergen, PPD, and the Frei test were negative. There was a 10 by 10 mm. reaction to the toxoplasmin skin test. Sabin dye test (reported later) was 1:64.

The patient was treated with local mydriatics and cortisone drops. On February 21st, the visual acuity was 20/100. There was essentially no change in the eye. He was started on Daraprim® (26 mg., twice daily) and sulfadiazine (0.5 gm., twice daily).

On February 26th, the vision was 20/60. There was slightly less reaction in the anterior chamber.

On February 28th, the Daraprim® was cut to 25 mg. every day and the sulfadiazine to 0.5 gm. every day.

On March 4th the Daraprim® was cut to 25 mg. every other day and the sulfadiazine to 0.5 gm. every other day.

On April 13th, the vision was 20/30. The vitreous opacities were less dense and the lesion showed beginning pigmentation.

On April 20th, the Daraprim® and sulfadiazine were discontinued.

On May 3, 1955, the vision was 20/30. The vitreous opacities were less and the lesion appeared healed. The patient was discharged.

CASE 4

History. M. I. P., a 21-year-old white woman, was first seen in the eye clinic on March 28, 1955. One week previously she began to notice small black spots in front of her right eye. These became worse and were accompanied by some redness and pain in the eye.

Ocular examination. The visual acuity was correctible to 20/50 in the right eye and to 20/20 in the left. In the right eye there was moderate circumcorneal injection, there were scattered mutton fat keratic precipitates, and two-plus flare and cells were present in the anterior chamber. There were considerable vitreous opacities partially obscuring the fundus details. About four disc diameters temporal to the disc there was visible a large white fluffy area of acute chorioretinitis. The left eye was normal to slitlamp and ophthalmoscopic examination. The intraocular pressure was normal in each eye.

Uveitis survey. CBC, urinalysis, Kahn, agglutinations to Brucella, and total serum protein and A/G ratio were normal or negative. Skin tests to histoplasmin, coccidiodin, and PPD (first, intermediate, and second strengths) were negative. There was a 20 by 20 mm. reaction to the toxoplasmin skin test. The Sabin dye test (reported later) was 1:16.

On April 1st, the visual acuity had diminished to 5/200 in the right eye. There was more injection and the mutton fat keratic precipitates were much more marked. She was started on Daraprim® (25 mg., twice daily) and sulfadiazine (0.5 gm. four times daily).

On April 8th, there was less injection and the keratic precipitates were becoming crenated. The visual acuity, aqueous flare, and vitreous opacities remained the same. She was started on cortisone (25 mg., four times daily).

On April 11th, the keratic precipitates were almost gone. There was no other evidence of improvement. The Daraprim® was cut to 25 mg. every day.

On April 27th, the visual acuity had improved to 20/80. There was still a plus-two flare and heavy vitreous opacities. The Daraprim was cut to 25 mg. every other day, the sulfadiazine to 0.5 gm., twice daily, and the cortisone to 25 mg., twice daily.

On June 18th, the vision was the same. There was only a plus-one flare. Beginning pigmentation of the lesion was noted. The Daraprim® was discontinued. The cortisone was also discontinued gradually.

On August 15th, the visual acuity was 20/60. There was still a plus-one flare. The vitreous opacities were somewhat less and there was further pigmentation of the lesion. The sulfonamide was discontinued and she was begun on Daraprim® (25 mg., twice a week).

On December 3rd, visual acuity was 20/40. There was only plus or minus flare and the vitreous opacities continued to clear. There was marked pigmentation of the lesion and no signs of activity except slight surrounding retinal edema. The Daraprim® was cut to 25 mg. every week.

CASE 5

History. A. W. LaS., a 27-year-old white man, was admitted to the U. S. Naval Hospital, San Diego, California, on August 31, 1955. He said that his left eye had been red and his vision had been blurred for the past four or five days. There was no history of previous eye disease.

Ocular examination. The vision was 20/20 in the right eye and 20/80 in the left. The right eye was normal to slitlamp and ophthalmoscopic examination. Examination of the left eye revealed moderate deep injection, many mutton fat keratic precipitates, and plus-two flare and cells. There were thick, syrupy vitreous opacities partially obscuring fundus details. There was visible a large fluffy area of fresh chorioretinitis extending from the disc inferonasally on both sides of the inferior nasal branches of the vessels. Just peripheral to this lesion, there were two smaller heavily pigmented healed lesions.

Uveitis survey. The following were normal or negative: CBC, Kahn, urinalysis, fasting blood sugar, agglutinations to Brucella, total serum proteins and A/G ration, and X-ray films of the chest. Skin tests to histoplasmin, coccidiodin, Frei test, and PPD in all dilutions were negative. There was a 22 by 24 mm. reaction to toxoplasmin. Sabin dye test (reported later) was 1:64.

On September 3rd, he was started on Daraprim® (25 mg. three times daily), sulfadiazine (0.5 gm., four times daily) and cortisone (25 mg., four times daily).

On September 8th, the Daraprim was cut to 25 mg. twice daily.

On September 10th, the vision was 20/60. There was only slight injection and the keratic precipitates had become crenated and were resolving.

On September 14th, the vision was 20/50. There was a plus-one flare and the keratic precipitates were continuing to resolve. The Daraprim® was cut to 25 mg. every day.

On September 24th, the vision was 20/40. The cortisone was cut to 25 mg., three times daily for three days and then to twice daily.

On September 27th, the Daraprim® was cut to

25 mg. every other day, and the sulfadiazine to 0.5 gm., twice daily.

On October 3rd, the cortisone was cut to 25 mg. every day.

On October 5th, the cortisone and sulfadiazine were discontinued. Daraprim® was cut to 25 mg. twice a week.

On October 24th, the vision was 20/100 and the fatty keratic precipitates were present again. He was started on Delta Cortef (5.0 mg., four times daily) for four days and then 5.0 three times daily).

On October 24th, the vision was 20/70 and the keratic precipitates were becoming crenated again.

On November 14th, the vision was 20/40. There was a plus or minus flare and the keratic precipitates were largely resolved. The Delta Cortef was cut to 5.0 mg., twice daily.

On November 28th, the vision was 20/30. The keratic precipitates were gone and there was only a plus or minus flare. The posterior vitreous opacities were still present. The area of chorioretinitis showed definite evidence of healing with early beginning pigmentation.

CASE 6

History. R. O., a 19-year-old white man, was admitted to the U. S. Naval Hospital, San Diego, California, on August 29, 1955. He said that about three weeks prior to admission the vision in his right eye had become blurred and that the eye had been red and slightly painful. There was no history of injury or previous eye disease.

Ocular examination. Visual acuity was limited to light perception in the right eye and was correctible to 20/20 in the left eye. There was marked deep injection in the right eye. The pupil was irregular. There was a plus three flare and cells and several large mutton-fat keratic precipitates were present. There were complete posterior synechia. No fundus details were visible because of the dense vitreous opacities; however, there was discernible a large exudative lesion above the macula. Slitlamp examination of the left eye was negative. Below the left macula there were three heavily pigmented healed chorioretinal lesions. The intraocular pressure was 29 mm. Hg in the right eye and 17 mm. Hg (Schiøtz) in the left.

Uveitis survey. The following were normal or negative: CBC, Kahn, urinalysis, fasting blood sugar, agglutination for Brucella, and total serum proteins and A/G ratio. The chest X-ray film was negative. Skin tests to PPD, histoplasmin, coccidiodin, and the Frei test were negative. There were 35 by 40 mm. reaction to toxoplasmin. Sabin dye test (reported later) was greater than 1:1024.

On September 1st, he was started on Daraprim® (25 mg., twice daily), sulfadiazine (0.5 gm., four times daily), and cortisone (25 mg. four times daily).

On September 3rd, there was a generalized urticaria and the sulfadiazine and Daraprim® were discontinued.

On September 4th, under the supervision of the dermatology consultant he was started again on Daraprim® and sulfadiazine and also given 25 mg. Benadryl (four times daily). The urticaria cleared and there was no further skin reaction.

On September 6th, the vision was counting fingers at two feet. The keratic precipitates were becoming crenated. There was a plus-two flare, the posterior synechia was no longer present, and there was only mild deep injection. The Daraprim® was cut to 25 mg., twice daily.

On September 12th, the Daraprim® was cut to 25 mg. every day.

On September 24th, the cortisone was cut to 25 mg. three times daily.

On October 3rd, the cortisone was cut to 25 mg. twice daily, and gradually decreased until October 5th, at which time it was discontinued completely.

On October 6th, the Daraprim® was decreased to 25 mg. every other day and the sulfadiazine to 0.5 gm. twice daily.

On October 17th, the Daraprim® was cut to 25 mg. twice weekly.

On October 1st, the Daraprim® was decreased to 25 mg. every week.

On October 24th, the sulfadiazine and Benadryl were discontinued.

On November 28th, the vision was 2/200. There was no injection and the pupil was nicely dilated. There was still present a plus-two flare and cells and a few crenated keratic precipitates. The vitreous opacities were still very dense obscuring the details of the fundus. However, there were still visible a large whitish lesion above the right macula.

CASE 7

History. J. D. S., a 21-year-old white man, was admitted to the U. S. Naval Hospital, San Diego, California, on September 6, 1955. He said that for the past month his left eye had been red and had "scratchy feeling." There was no history of trauma or previous eye disease. His father had died of tuberculosis in 1943 and one brother had "something wrong with his lungs."

Ocular examination. The visual acuity was 20/20 in each eye. There was mild deep injection of the left eye. There were multiple small greasy keratic precipitates in the left eye and a plus or minus flare and cells. There was no choroidal lesion visible after careful examination with direct and indirect ophthalmoscopy. The right eye was normal to slitlamp and ophthalmoscopic examination. Intraocular pressure was normal in both eyes.

Uveitis survey. The following were normal or negative: CBC, Kahn, urinalysis, fasting blood sugar, agglutionations for Brucella, total serum proteins and A/G ratio. The chest X-ray film revealed an old healed complex but no active disease. Skin tests to histoplasmin, coccidiodin and the Frei test were negative. The PPD was negative in first and intermediate strength. There was

a plus-three reaction to second strength PPD. There was an 18 by 22 mm. reaction to toxoplasmin skin test. Sabin dye test was 1:256.

On September 19th, the patient was started on Daraprim® (25 mg., three times daily) and sulfadiazine (0.5 gm., four times daily). The Daraprim® was cut to 25 mg. twice daily after four days and then to 25 mg. once daily after another week. The sulfadiazine was discontinued on October 4th.

On October 13th, the Daraprim® was decreased to 25 mg. every other day, on October 17th, to 25 mg. twice weekly, and on October 29th, to 25 mg. once a week. On October 29th, the sulfadiazine was discontinued and the visual acuity was still correctible to 20/20 in each eye. There was no change in the keratic precipitates and the plus or minus flare was still present.

On November 22nd, there was still no change in the eye and the Daraprim® was discontinued.

CASE 8

History. P. G. S., a 24-year-old white woman, was first seen in the eye clinic August 15, 1955. She had been treated elsewhere the year before with streptomycin, PAS, and cortisone for a choroiditis of the left eye. Her vision had continued to be blurred in this eye and the eye remained mildly inflamed.

Ocular examination. The visual acuity was 20/20 in the right eye and 20/200 in the left. There was mild circumcorneal injection of the left eye. There were no keratic precipitates but there was a plus-one flare and cells and several posterior synechia were present. There was a saucer-shaped posterior cortical lens opacity in the left eye. The intraocular pressure was 17 mm. Hg, O.U. The fundus of the left eye was blurred because of the lens and vitreous opacities. There was visible one large and two small areas of heavily pigmented healed chorioretinitis temporal to the macula and a small fresh lesion between the healed lesions and the macula. The right eye was normal to slitlamp and ophthalmoscopic examinations.

Uveitis survey. The following were normal or negative: CBC, Kahn, urinalysis, agglutinations to Brucella, and total serum proteins and A/G ratio. The chest X-ray films revealed numerous calcific densities which were interpreted as a healed primary complex (however, she had been told elsewhere that she had the X-ray findings of healed histoplasmosis). The skin tests were negative to coccidiodin, Brucellergin, PPD in all dilutions, and the Frei test. There was a 20 by 20 mm. reaction to toxoplasmin and a 25 by 30 mm. reaction to histoplasmin.

On September 26th, there was no change in the vision or in the appearance of the eye (the patient had been on local mydriatics and hydrocortisone drops). She was started on Darapim® (25 mg., three times daily), sulfadiazine (0.5 gm., four times daily), and cortisone (25 mg. four times daily).

On September 30th, the vision was 20/100 in the left eye. Slitlamp and ophthalmoscopic appearance were unchanged. The Daraprim® was cut to 25 mg., twice daily for three days and then to 25 mg. every day.

On October 5th, the vision was 20/100. The patient said that the black spots were much less noticeable. There was only a plus or minus flare and the lesion appeared "less fresh" with the ophthalmoscope. The Daraprim® was cut to 25 mg. every other day. The cortisone was cut to 25 mg., three times daily for five days, and then to 25 mg., twice daily.

On October 19th, the visual acuity was 20/80 and the patient continued to notice subjective improvement. The Daraprim® was cut to 25 mg. twice a week and the sulfadiazine to 0.5 gm. twice daily.

On October 26th, the Daraprim® was cut to 25 mg. every week and the cortisone to 25 mg. every day.

On November 28th, the vision was 20/70. There was only a plus or minus flare. There was no change in the secondary cataract. The retinal lesion appeared completely quiet. Although there was only slight pigmentation, there was no edema and no "fresh" appearance. The sulfadiazine and cortisone were discontinued. The Daraprim® was continued at 25 mg. per week.

CASE 9

History. M. D. McC., a 12-year-old white boy, was admitted to the U. S. Naval Hospital, San Diego, California, on November 4, 1955. The history is a little indefinite, but there had been some visual difficulty for about two years. This became much worse in the summer of 1955. He was admitted to Wills Eye Hospital in Philadelphia, on September 16, 1955. At that time the visual acuity was 5/60 in both eyes. He had a bilateral disseminated chorioretinitis with vitreous opacities and with bilateral pallor of the discs. At Wills he was treated with systemic penicillin, streptomycin, oral Daraprim,® and triple sulfa. He was also given fever therapy and intramuscular ACTH. His father was transferred to San Diego and he was discharged from Wills on September 29, 1955. At that time his vision was 6/60 bilaterally.

Ocular examination. The visual acuity was 9/200 in the right eye and 14/200 in the left eye. There were no keratic precipitates, cells, or flare in either eye. There were many fine vitreous opacities in both eyes. There was moderate waxen atrophy of both discs. There were bilateral heavily pigmented lesions in both macular areas. There was moderate retinal edema in both macular regions. In both eyes there were also multiple heavily pigmented annular lesions about one third the size of the disc. These lesions were scattered throughout the posterior segment and had no appearance of activity.

Uveitis survey. CBC, Kahn, and urinalysis were negative. Skin tests to PPD in all dilutions, histoplasmin, coccidiodin, and the Frei test were nega-

tive. There was a 10 by 12 mm. reaction to the toxoplasmin test.

Patient was treated with Daraprim® (12.5 mg. twice a week).

At the time of his discharge from the hospital on November 25, 1955, the ophthalmoscopic examination of his eye was unchanged except that there was perhaps less retinal edema in the macular areas. The visual acuity at discharge was 11/200 in the right eye and 20/200 in the left eye, correctible in the left eye to 20/80 — 2 with a pinhole disc. He is continuing Daraprim® (12.5 mg. twice a week) as an out-patient.

Summary

1. Nine cases of presumptive toxoplasmic uveitis were treated with Daraprim® and sulfadiazine. The period of treatment ranged from one month to 10 months. Some of these patients are still receiving treatment.

2. Three of these patients showed marked improvement within a week and continued to quiescence of their lesion.

3. Four of the patients showed improvement varying from slight to marked over a longer period of time.

4. One patient showed no response to therapy and in retrospect should probably not have been included in the group. Although the only finding on his uveitis survey was a positive toxoplasmin skin test, his father had died from tuberculosis, and his disease was confined to the anterior segment (iridocyclitis).

5. There were no severe toxic reactions from the use of these drugs.

Conclusions

1. The response of four cases (1, 2, 3, and 8) to treatment with Daraprim® and sulfadiazine was striking and was much more rapid than would be expected unless the response was the direct result of treatment.

2. Four other cases improved while under treatment with Daraprim® and sulfadiazine. To the observers, this improvement seemed to be related to the treatment. However, it is possible that this may have been the normal course of the disease in these patients.

3. Although the toxoplasmic etiology of adult chorioretinitis has been proven, our diagnostic methods are fallible and in most cases the diagnosis of toxoplasmic chorioretinitis must be presumptive at best.

4. The average ophthalmologist, not associated with a research facility, does not have available repeated serial Sabin dye tests. The combination of careful history and examination of the patient, a thorough attempt to rule out other granulomas as an eitiology, plus a positive skin test to toxoplasmin is probably his best approach to making a presumptive diagnosis of toxoplasmic chorioretinitis.

5. The decision to treat or not to treat a case of presumptive toxoplasmosis should be made by the individual ophthalmologist and should probably be based partly on the severity of the case. It certainly should not be begun without adequate supervision in regard to possible toxic effects from these drugs.

6. Although there were no severe reactions to Daraprim® and sulfadiazine in the small series which we have reported, toxic reactions including temporary but severe depression of the hematopoetic system have been reported by others.

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DEVELOPMENTAL ANOMALIES OF THE LACRIMAL PASSAGES*

A REVIEW OF THE LITERATURE AND PRESENTATION OF THREE UNUSUAL CASES

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Because developmental anomalies of the lacrimal passage are as interesting as they are rare, a summary of conditions to be found and a review of the literature are included with the following case presentations. The three cases illustrate somewhat unusual combinations of anomalous conditions. The summary and review are presented as an orientation, and are not meant to be exhaustive.

A REVIEW

Absence or atresia of the canaliculus and punctum. This condition would appear to be relatively rare. Goar,[1] in 1931, gave a review of the literature up to that time and stated that the condition was found but once in Mooren's series (cited by Burnett[2] of 108,416 examinations. Goar then reviewed cases presented by Blanchet,[3] Zehender,[4] Emmert,[5] Magnus,[6, 7] Von Ruess,[8] Fieugal,[9] DeWecker and Landolt,[10] Cabannes,[11] Fox,[12] Ferron,[13] Lafite,[14] Lebeque[15] (who reviewed the literature up to that date and described five cases), Kraupa[16] (who also reviewed the literature), Gradle,[17] and Blackmar.[18] Goar then added a case of his own. In all, the cases totalled 23.

It appeared that in most, if not all, cases investigated surgically, the canaliculi were absent when the puncta were absent. When there was some external evidence of a rudi-

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mentary punctum, the canaliculus often was present and patent.

Thus in Blackmar's report of a case,[18] he states, "There was no superior or inferior punctum demonstrable in either eye, although their normal situation was indicated by slight smooth elevations on the lower lids only. An attempt was made with a Graefe knife to open a possible hidden canaliculus." (This was not found.)

Cameron,[19] in 1934, presented a case in which ". . . the upper and lower lids in each eye were normal in every respect except for the absence of puncta. There was no indentation at the usual site of the punctum, nor was there any abnormality along the course of the canaliculi. Dissection at the time of operation failed to reveal any lower canaliculi. . . ." (The upper lids were not dissected.)

Guy,[20] in a similar case report, found no punctum present in either the upper or lower left eyelid and when the left lacrimal fossa was exposed and explored no lacrimal sac, canaliculus, or other structure of the lacrimal apparatus was found.

Atresia of the punctum. Atresia of the punctum alone is apparently not so uncommon an occurrence, and a considerable number of cases have been reported over the years.[21]

Anomalies in shape and position of the puncta. These are less often seen, and the reported cases include variations in appearance of the punctum, variations in length, congenital ectopia of the puncta, eversion, and so on.

Supernumerary puncta and canaliculi. These form a somewhat intermediate group. Mann[22] states the condition is not rare. Bothman,[23] in 1932, presented a review of the literature in regard to cases exhibiting double puncta and canaliculi. He cited Rosenblatt,[24] who in 1929 reported six cases of double puncta of the lower lid. Rosenblatt in his report also stated that Stock[25] had cited only one case up to that time from the world literature (that is, prior to 1925). In 1901, Schoute[26] gathered 22 cases of double puncta from the published reports and added one of his own. Cosmettatos[27] gathered an additional 18 cases, but was indefinite as to which lid was involved. Cases were reported by Majewski,[28] Greeves,[29] Hertz,[30] Chase,[31] and Iolfe.[32] As far as frequency is concerned, Wicherkiewicz[33] noted supernumerary puncta and canaliculi once in 60,000 cases. Kleczkowski,[34] in a rather remarkably similar statement, found only two cases of tear passage anomalies in 120,000 cases.

Embryology

The lacrimal passages are described as developing along with the facial fissure, and the primordium of the tear ducts lies in a solid rod of cells which is derived from surface ectoderm and becomes situated in the groove between the lateral nasal and maxillary processes at about the 10-mm. stage (Wolff). At the 15-mm. stage it is free from the ectoderm, and grows upward into the lids to form the canaliculi. The canaliculi and puncta are thus the result of out-budding from the upper end of this rod, the lower portion going to form the passageway into the nose.

Anomalies which may develop thus follow the forms of the embryological development, so that the sac and ducts may fail to bud off from the rod of surface ectoderm cells, the ducts may run in the wrong direction, they may eventually fail to canalize, or there may be extra rods of cells budding off the original rod thus forming supernumerary canaliculi and puncta. Whitnall[35] gives a concise description of this process, and Fischer[36] gives a detailed and somewhat theoretic approach to the formation of the entire lacrimal apparatus.

Case presentations

Case 1

A 43-year-old white woman, in good health, was seen primarily because of a conjunctivitis, and the anomalous develop-

ment of the lacrimal apparatus was noted as an incidental finding. It had not been noticed previously by the patient, had caused no discomfort or epiphora, and was not present in other members of the family.

Examination of the eyes revealed a normally placed punctum on the lower lid of the right eye with another punctum, somewhat slitlike in appearance and measuring about 1.5 to 2.0 mm. in length, situated about 2.0 mm. nasally from the first along the lid margin (fig. 1).

When a probe was inserted into the normally situated punctum (A in fig. 1), the vertical portion of the canaliculus was found to extend somewhat deeper into the lid than would normally be expected, but the horizontal portion coursed normally along in the lid and into the sac, and the probe could be passed from thence easily into the nose.

A probe inserted into the nasally placed punctum (B in fig. 1), was found to enter another canaliculus which was situated very close to the skin surface of the lid margin, but which, nevertheless, ran along parallel with the deeper duct until they joined somewhere in the region of the canthal ligament or beyond. Probes were inserted simultaneously into the two ducts and an X-ray film was taken (fig. 2).

Fig. 1 (Kirk). Inner canthus of right eye, showing double puncta of lower lid.

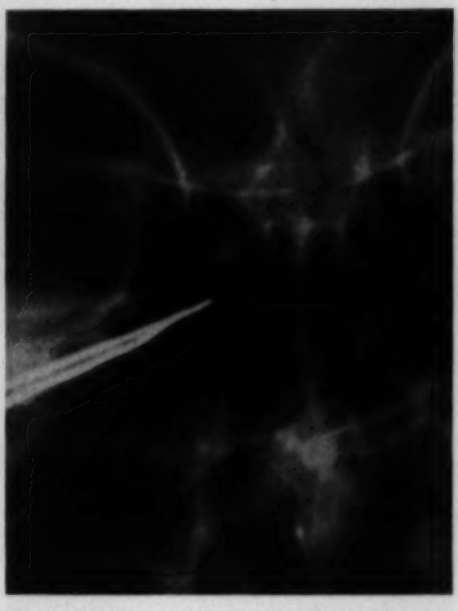

Fig. 2 (Kirk). Anteroposterior X-ray film, with probes in place in the reduplicated canaliculi.

In addition, an X-ray film was taken after the injection of lipiodol into the upper, anomalous duct (fig. 3). This demonstrated very well the horizontal portion of the duct (H), and showed how it ran into the sac (S). It was impossible to demonstrate by X-ray examination any delineation of the two ducts when they were simultaneously injected with lipiodol, as they blended into one opaque line. A lateral view presented very well the lipiodol in the sac, and outlined the valves (fig. 4).

An examination of the upper lid of the same eye revealed no punctum, and no rounding or indentation at the usual site of the punctum. The skin in this area was quite smooth (fig. 5). Probing and X-ray examination with lipiodol with the patient in a head-down position for a short period failed to show any evidence of a canaliculus.

We may assume in the present instance, therefore, that in the embryo both canaliculi budded off the parent rod of cells, but that instead of one going to the upper lid and

Fig. 3 (Kirk). Anteroposterior X-ray film, showing the injected lipiodol in the canaliculus and sac.

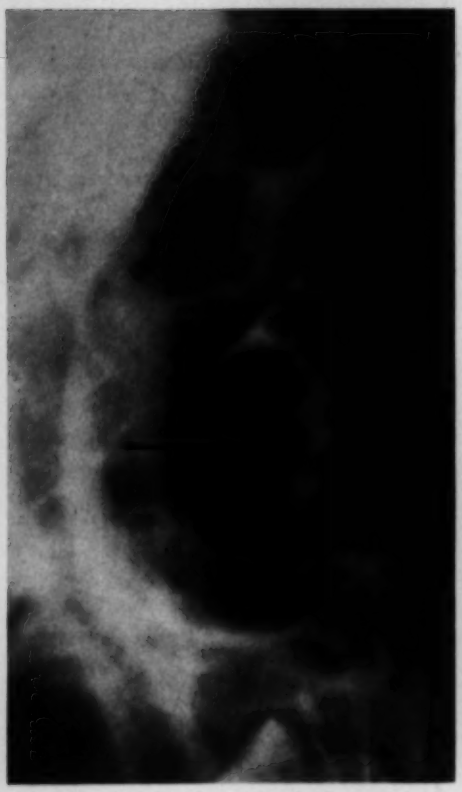

Fig. 4 (Kirk). Lateral X-ray film, showing the lipiodol in the sac.

one to the lower, both grew into the lower lid. This allowed the caruncle to form normally, and presented the picture of a reduplicated punctum and canaliculus of the lower lid, with an absent punctum and canaliculus of the upper lid. We thus have an unusual form of supernumerary puncta, the more usual type being that of a normal punctum on the opposing lid with the lower budding cells splitting to form a duplicated passage.

Fig. 5 (Kirk). Upper lid of right eye showing absence of punctum.

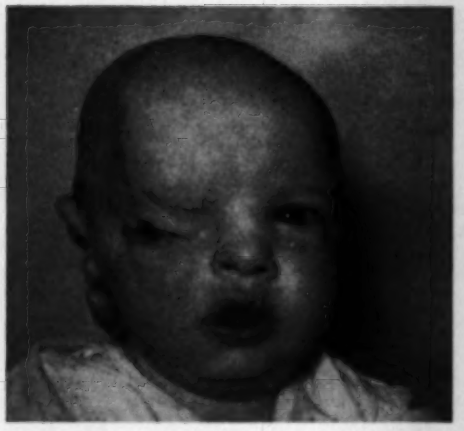

Fig. 6 (Kirk). Full-face view showing anomalies in region of right orbit.

CASE 2

This patient, a 32-year-old white man, showed a reduplicated right lower punctum and canaliculus, identical in appearance and formation to Case 1 except that a normal punctum and canaliculus were present in the upper lid. Examination with probes indicated that the reduplicated ducts joined to a common duct before joining the upper, normally placed canaliculus. In this instance, also, there were no symptoms referable to the tear ducts, and the ducts of the left eye were normal.

CASE 3

The third case presented a group of anomalies, all of them being on the right side of the face in the region of the right orbit (fig. 6). The patient, a white boy, was seen for the first time at the age of five months. The anomalies had been present from birth and included the congenital absence of bones of the skull in the frontal, maxillary, and orbital areas on the right. The right frontal lobe was covered only by meninges and skin. Because of the absence of supporting orbital bone, the eye had become displaced downward and outward onto the cheek. It could be moved in all directions and, therefore, the extraocular muscle mechanism was assumed to be essentially normal. A large coloboma was present in the upper lid, there was an absence of punctum and canaliculus of the upper lid, and in the lower lid there were four puncta all in a row (fig. 7).

As well as could be determined, two canaliculi were present, one on top of the other, with two puncta to each. The other eye and lids were entirely normal, and the baby was an entirely normal, healthy boy otherwise.

Fig. 7 (Kirk). Inner canthus of right eye showing four puncta in a row on lower lid, and absent punctum on upper lid.

SUMMARY

A review of the literature pertinent to anomalies of the tear duct passages is presented.

Three cases showing unusual combinations of these anomalous findings are reported.

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Ophthalmic Miniature

He (Tuberville) cured several who were blind but I do not look upon that as so great a thing for the cure of such curable, for there are several sorts of cataracts uncurable, it consists wholly in viz., to know when the connate cataract is fit to be couched, in having a steady hand and skill to perform that operation, to be able to prevent or at least remove the pain which usually follows and sometimes kills the patient; but to reduce the fallen or inverted eyelids to their proper place and tone, to cure inveterate ulcers and inflammations of blackish colour requires a consummate artist, *Hic labor hoc opus est.*

Dr. Walter Pope,
Memoir of Bishop Seth Ward, 1697.

PHYSIOLOGY AND PATHOLOGY OF THE OPTOMOTOR REFLEXES*

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I. DEVELOPMENT OF THE OPTOMOTOR REFLEXES

It is customary to divide the ocular movements into reflex and voluntary movements. This, however, does not by any means exclude the possibility that a reflex character must be ascribed also to the so-called voluntary movements. As early as 1889, it was emphatically pointed out by Wernicke, and 10 years later also by Reddingius (1899) and Roux (1899), that such a reflex character existed. The present opinion that the "spontaneous" movement of the eyes has developed as a higher conditioned reflex with the aid of associative links is constantly gaining ground.

Ocular reflexes can be evoked by nonoptical, as well as by optical, stimuli. Long before birth the eyes are already involved in reflex movements by nonoptical stimuli, partly as a result of local—proprioceptive—stimuli which give rise to monocular reactions, and partly by stimuli from more remote parts—vestibular and musculosensory—which give rise to conjugate (binocular) reflexes.

After birth and the entry of light into the eye, optical stimuli will now also act on an apparatus that has so far been governed chiefly by tonic reactions from the co-ordination centers. From now onward these centers will also receive optical stimuli, which on the one hand will alter the tonic innervation and on the other hand will evoke dynamic reactions. Conversely, these dynamic reactions will in turn give rise to the occurrence of fluctuations in tonus in the co-ordination centers as a result of the displacement of contours over the retina. There will thus be a varying reciprocal influence of these tonic and dynamic reactions, in the form of inhibition or activation.

And how are we to imagine the development of these optomotor reflexes as taking place? It seems obvious in this connection to take the light stimulus as the conditional stimulus which, as in Pavlov's experiments, under certain conditions and in certain circumstances, will give rise to the development of certain optical reactions as conditioned reflexes.

This implies, then, that the younger optical reflexes are assumed to be built up as superposed reactions on the older, nonoptical ocular reflexes.

Chavasse (1937) as well as Zeeman (1943), both of whom have worked out theories as to the origin of the reflexes leading to ocular movements, took this premise as their starting point. Chavasse, however, made the mistake of taking exclusively the compensatory reactions as the unconditioned basis upon which these reflexes will develop, so that he was compelled to derive all optomotor reactions from conjugate innervations. This also compelled him to deny categorically the existence of monocular innervations in man and animals. It is now quite clear that this idea was incorrect.

Zeeman's contribution has been the extension of Pavlov's concept that the conditioned—chiefly cortical—reflexes develop during the individual existence out of the unconditioned—chiefly subcortical—reflexes. This extension consists primarily in placing the action of the manifestation of the individual life itself at the center of events.

This led him to assume that every reflex, thus also the so-called unconditioned reflexes, originally started, partly in an ontogenetic sense, as a conditioned reflex. The oldest reflex of all might thus have been "grafted

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† Deceased.

onto a chance spontaneous event—onto an individual initiative of the life in the course of self-expression." The neurobiotaxis (Ariëns Kappers) might be able to indicate an anatomic basis for the further development of the conditioned reflex.

As unconditioned bases upon which the optomotor reflexes are grafted, Zeeman takes the two forms in which the reflex eye movements evoked by nonoptical stimuli are manifested: one of these is the monocular reflex evoked by proprioceptive impulses emanating from the ocular muscles (and their immediate surroundings) of each eye separately, and the other comprises the conjugate, compensatory reflexes which are evoked by vestibular and musculosensory stimuli from the labyrinth and the neck muscles respectively.

From these two substrata the optical reactions will now develop, with the aid of the light stimulus, as conditioned reflexes. We can thus distinguish the following groups:

a. Monocular optomotor reflexes; these are grafted onto proprioceptive reflex pathways.
b. Conjugate optomotor reflexes, which are grafted chiefly onto vestibular reflex pathways.

The convergence reflex we consider to be grafted, in the last analysis, on the proprioceptive reflex pathway.

Zeeman assumes that the displacement of images over the retina which occurs in monocular and conjugated ocular movements must be regarded as the conditional stimulus which calls the optomotor reflexes into being. While the proprioceptive (monocular) reflex endeavors to maintain the original position of the eye in the orbit, the compensatory (conjugate) reflexes strive to fix the position of the eye with respect to the external world. The optical reactions grafted into these lower reflexes will also act in the same direction and thus tend to prevent any displacement of the image on the retina. It will therefore be possible for them to be evoked from peripheral as well as central parts of the retina and in this way they have become optical fixation reflexes ("Einschappmechanismus"; Kestenbaum, 1921).

Owing to the fixation tonus produced by them they will make an important contribution to the maintenance of the optical gaze tonus. This means that on the one hand they will cooperate in eye movements elicited by moving contours (slow phase of optokinetic nystagmus) but on the other hand also that they will not confine their influence to the eye movements but will also act as optical postural reflexes, in the sense in which this term is used by Magnus (1924).

In virtue of their origin, the monocular reflexes will contribute to the optical fixation reflex chiefly in the primary direction of gaze; in a secondary direction of gaze they will tend rather to co-operate in bringing the eye back to its "Grundstellung" (fundamental position) (Magnus 1924), at the same time also promoting the "Entspannungstendenz" (relaxation tendency) of Kestenbaum (1921). In this way they have come to form one of the components of the fast phase of optokinetic nystagmus.

The gradually developing functional predominance of the macula creates the conditions and the need for the development of an adjusting reflex. Gradually, by a process of grafting on and calibration by the proprioceptive and vestibular reflexes, a certain precisely graded impulse will be allotted to each part of the retina. If the eye is at rest we may assume that the resultants of all these optomotor impulses just balance each other and thus maintain a tension-pattern that will contribute to the optical gaze tonus. But as soon as a peripheral part of the retina acquires a certain preponderance, either in consequence of the strength or nature of the stimuli or via associative pathways, so that the other stimuli are inhibited, an adjusting movement will occur. Constant corrective impulses emanating from the fixation point are necessary to maintain the adjustment. These at the same time determine its optical localization.

The repeated coincidence of identical monocular and conjugate adjusting reflexes in both eyes, as evoked by the predominance of a given stimulus from the outside world, will give rise to ever-repeated simultaneous stimulation of corresponding retinal elements and will lead to the formation of a functional junction between the cortical representations of these retinal elements and finally between the entire homonymous retinal halves of the two eyes. This new motor link between the two eyes at the cortical level, which in man has its anatomic substratum in the semidecussation, we call the cortical binocular junction (Keiner, 1951), to distinguish it from the subcortical junction via the conjugate reflex pathways.

On the basis of this junction, identical adjusting reflexes will combine to give a single adjustment innervation: the impulse to an originally monocular eye movement has thus become an impulse to binocular eye movement, owing to the fact that when a certain retinal element is stimulated, not only its own cortical representative but also the cortical representative of one of the corresponding retinal elements will emit a motor impulse.

Purely binocular foveal adjustment with the aid of conjugate eye movements is impossible in most cases. Only by the addition of mutually opposed ocular movements can the desired result be fully achieved. If stimuli which command our attention impinge in the two eyes upon retinal elements whose cortical representatives do not possess a cortical junction, these stimuli will be unable to evoke a common optomotor impulse and the result will be that double images are seen. What can happen is that the two stimuli evoke two separate but equal convergence impulses, which, together with the still possible bilateral monocular adduction impulses, lead to the establishment of the correct adjustment (motor fusion). In this way the fusion of the two monocular impressions by a common innervation impulse is made possible (sensory fusion; Roelofs, 1926).

It is thus the cortical binocular junction that creates the possibility of a common innervation impulse and hence of a harmonious distribution of the impulses over the two eyes. Where such junction is absent (strabismus) Hering's law is also not valid.

A very interesting study, from a biologic point of view, of the possibility in the animal kingdom of junctions in the central nervous system with gradually increasing decussation of the optic fibers was published by Zeeman in 1949. Those interested are advised to read it.

It is obvious, in connection with smooth functioning and the repeated necessity for opposed ocular movements to give a good binocular adjustment, that the cortical binocular junction cannot be a point-to-point linkage. Every representative of a retinal element of one eye is linked to a group of representatives of retinal elements of the other eye. This finds its expression in the "Empfindungskreis" (perception circle or area) of Panum. In accordance with the extension of these perception circles, it is now possible for two monocular adduction impulses originating from a single point in the external world to unite to give a single (common) convergence impulse (Roelofs, 1943).

The area with which each cortical representative becomes linked up can be regarded as the anatomic substratum of the perception circle of Panum. The common convergence impulses which it makes possible form the physiologic correlate of depth perception.

Zeeman did not at first derive the convergence reflex from pre-existent optical reflexes but believed it to be grafted onto the increase of tonus that occurs in the whole complex of medianly situated flexor muscles —among which he also includes the internal recti muscles of the eye—upon the approach of a prey or enemy. He assumed that the place of the activating olfactory stimulus had gradually been taken over by the changes in size of the images and the oppositely directed displacement of the images, and finally

by the stimulation of disparate retinal elements. At a later date, however, he came to agree with Roelofs' suggestion that the convergence reflex had been built up—with inhibition of the innervation to right and left turning—out of a double adduction innervation.

If we now survey the development of the optomotor reflexes we are struck: first by the simplicity and secondly by the small number of reflex reactions that appear necessary for the correct adjustment and coupling of such a complicated optical apparatus. Only the adjusting reflex and the fixation reflex are indispensable for the harmonious maintenance or restoration of the repeatedly disturbed optical equilibrium in the multitudinous interrelationships between the individual and his environment.

All other optomotor reflexes, that is, the following movement (a combination of adjustment and fixation reflexes), the fusion reflexes (adjusting reflexes for opposed movements of the eyes), and the convergence reflex (a combination, which has become possible under certain conditions, of two adjustment [adduction] innervations) are derived from the above-mentioned fundamental or basic reflexes. The pupillary and accommodation reflexes are left out of consideration here as they are not eye-movement reflexes.

By virtue of their origin the optomotor reflexes will be capable of evoking both tonic and dynamic impulses. The tonic reflexes, which are chiefly concerned with maintaining the position of the eye, are of great importance from both the physiologic and pathologic point of view. The pathology of the optomotor reflexes occurs to a considerable extent in the field of the tonic innervations.

These must be regarded as postural reflexes of the eye, in the sense in which the term was used by Magnus (ocular postural reflexes). The study of the tonic innervations induced by optical stimuli in the eye muscles, the results of which have been reported by Roelofs in a number of publications, and to which I have also been able to contribute in the last few years, has gradually led to a theory (the innervation-tonus theory—see Part III) which must be regarded as an application and extension of Magnus' theory of the origin and distribution of tonic innervations in the muscular system.

These theoretical considerations have received very important support from the results of investigations carried out especially in recent years by a number of workers (Gutman, 1924; Jones, 1926; Bartels, 1927; Guernsey, 1929; Beasley, 1933; Bing Chung Ling, 1942; Keiner, 1951; Crone, 1952; Mesker, 1953). I have made a study of the development of the reflexes in 85 normal babies.

As regards the time at which the optomotor reflexes are manifested in man, I am inclined to regard the primitive, probably originally monocular adjusting reflex as the oldest. This may even be manifested immediately after birth. It was found that the fixation reflex usually does not appear until the end of the third month, although McGinnis (1930) claims to have seen it in neonates. But the absence or jerky course of the following movement in the first few months of life, as well as the still absent or markedly subnormal electroretinogram (Zetterström 1953) are against this.

In a normal development the conjugated optomotor reflexes show a marked predominance over the monocular reflexes. A certain degree of such predominance will remain throughout life. My experience, both with normal children and with those having reflex disturbances (myelogenesis retardata, strabismus, and nystagmus), indicates that the reflex apparatus is built up in a given, regular succession which is probably phylogenetically determined, in connection with which the gaze tonus will also gradually increase.

This tonus is originally very low in the newborn, in whom it has so far been fed exclusively by nonoptical stimuli. Experience has shown that this nonoptical gaze tonus

can be "educated" and raised partly by the action of optical stimuli.

Where the two eyes are unequal, it is possible to find that in the better or preferred eye the reflexes have developed better or reached a further stage than in the poorer eye. This shows not only that the reflex apparatus is built up gradually but also that the functional stimulus is indispensable to this process, so that the mechanism cannot be built up until after birth.

It is obvious that the possibilities of this building up and the speed with which it takes place will depend on the stage of development and maturation that has been reached by the optical and optical-associative centers and pathways at the time of birth. This is especially true of the cortical retina, the development of which will undoubtedly be correlated with that of the peripheral retina. In this connection it is interesting to consider particularly the linkages necessary for the transmission of impulses in order to ensure good function.

While the examination of normal and squinting babies showed us that a cortical *binocular* junction must form after birth, our nystagmus studies have brought out the fact that for a normal functioning of the reflex apparatus it is equally necessary that a cortical *monocular* junction of the cortical representatives of the retinal elements be built up. Only if these two junctions are intact can a normal reflex apparatus develop and the position and fixation of the eyes be guaranteed in all circumstances. The normal cortical junctions hold the secret of perfect binocular function and also the key to possible disturbances.

The problem of ocular imbalance is to a great extent the problem of the central junctions.

II. Disturbances in the development of the monocular optomotor reflexes

The process of development of the optomotor reflexes, as outlined in the foregoing, can suffer disturbances as a consequence of anomalies in the peripheral or in the central organ or in the connections between them. Such disturbances may impede or totally prevent the proper building up or functioning of the reflex reactions. The fact that various factors, either local or general, bodily or mental, may unfavorably influence a process of this kind need not be further dealt with here.

A developmental disturbance can, of course, occur in the field of the monocular or the conjugated reflexes and it is to be expected a priori that both substrata will be disturbed in their expressions, although perhaps to different degrees.

All these disturbances give rise to well-defined clinical pictures, but the interrelationship of these has up to the present not been recognized, so that they are still generally regarded as separate clinical conditions and are classified and treated accordingly.

It goes without saying that the possibility of gathering together these separate clinical entities in a single group—that of the developmental disturbances of the optomotor reflexes—each being allotted its correct place in the group, will not only make these affections much easier to survey but will also be of great benefit to our theoretical understanding and practical treatment of them.

The fundamental building up of the optical reflexes begins very soon after birth and appears to go a great part of the way toward completion in the first six months of life, being further extended and perfected in the subsequent years. Therefore unfavorable factors which are present at an early age will give rise to more extensive and profound disturbances in the development of the reflexes than will anomalies which occur at a later date.

The course of development of the reflexes justifies, in many cases, the idea that retardations in the normal building up of tracts and synapses underlie the disturbances and that it is only rarely necessary to consider the action of a pathologic agent. In this also lies the possibility of a spontaneous correction of the disturbance, which is entirely in accordance with everyday clinical experience.

Little is known as yet of the point of action of the disturbances. In all probability this does not lie in the retina, as indicated by the electroretinogram (Keiner, 1951) and by studies on dark adaptation (Wald and Burian 1944). Electroencephalographic studies on strabismus patients with amblyopia (Levinson and Stillerman, 1950, 1951; Keiner, 1951; Burian and Watson, 1952; Dyer and Bierman, 1952; and Gerald Parsons-Smith, 1953) have provided some evidence which appears to support the idea that the affection must be sought in the occipital pole.

The disturbances are manifested in the form of a relatively excessive or insufficient tonic innervation, according to whether one considers the agonist or the antagonist. From the point of view of pathogenesis it seems more correct to speak always of a deficiency of innervation impulses. The reactions which consequently run chiefly in one direction will then secondarily raise the tonus of the antagonist.

The controversy as to whether monocular eye movements occur in man has long remained unsettled. Although their existence was denied by Hering (1868) and by Chavasse (1939), they were actually described as early as 1877 by Raehlman and Witkowsky. The number of observations increased gradually in the course of years (Preyer, 1895; Bühler, 1918; Gutman, 1924; Taylor-Jones, 1927; Guernsey, 1929; Beasley, 1933; Ling, 1942; Keiner, 1951; and Crone, 1952) while Bielschowsky also recognized their existence in 1904. Crone concludes, on the grounds of a study of the literature, that in infants the optical reactions develop, in part at least, on the basis of monocular movements and that the adjusting movement is originally a monocular optomotor reaction. Zeeman regards the monocular reflex as the basis of the optomotor system.

In addition to their occurrence in normal infants, monocular eye movements are also observed in cases of strabismus and myelogenesis retardata (Keiner), monocular nystagmus, unilateral amblyopia, spasmus nutans, blindness, and unilateral gaze spasm ("Schau-anfall"). The unilateral vertical eye movement and monocular nystagmus can be regarded as proof of monocular movements.

All this, however, does not alter the fact that we are still very far from having reached general agreement and that many people still adhere to the view expressed by Chavasse.

Recent investigations by Keiner (1951) and Crone (1952), however, have shown quite clearly that this view needs revision. These workers succeeded in showing that strabismus and alternating hyperphoria must have their origin in an imbalance of the monocular optomotor reflexes. Crone was able to confirm for vertical squint the conclusions reached by Keiner in connection with horizontal squint (p. 138). A more detailed account of these two investigations will now follow.

A. Strabismus

In a clinical and statistical investigation of 656 cases of strabismus convergens in children between the ages of zero and seven years (of whom 50 were under one year, 123 under two years, and 344 between two and four years), I found that in 18.44 percent of cases the squint had appeared very soon after birth (so-called "congenital" squint); in 34.60 percent it had appeared during the first six months of life; in 19.36 percent in the second six months; in 15.24 percent between 12 and 18 months; and in 9.15 percent between 18 months and two years. For the next half year the percentage dropped to 6.71 percent, followed by 1.98 percent at the age of three years, and only 0.91 percent at five years. Thus 53.94 percent of these children already had a constant squint at the end of their first year of life, while in 78.33 percent the squint was present by the end of the second year. In contradistinction to the current opinion that squinting starts between the second and fourth years in the majority of cases, the age of inception of the squint was found to be under one year in 54 per-

cent of cases, while more than 18 percent of these children had shown a constant squint a few days after birth. The literature of the last 40 years has confined itself to remarking that this "congenital squint" is rare.

These statistical findings have since been confirmed by Scobee and Nordlöw. Scobee (1951) found the anomaly to be "congenital" in 27.4 percent of 456 patients, while in 55 percent it had appeared during the first year. Nordlöw (1953) states that of 485 cases of squint before the age of 10 years, 50.9 percent had developed in the first year. As the difference is smaller than the standard error as calculated by Nordlöw, we may take it that the percentages found are in good agreement.

This early beginning has its consequences and it was this that led me to important conclusions with respect to the etiology and nature of strabismus. At this early age it was no longer possible, on anatomic and physiologic grounds, to consider refraction and fusion as etiologic factors. All attention had now to be turned to disturbances in the physiologic establishment of the optomotor reflexes, a process that is in full swing in this period of life. This idea also carried implications with regard to the nature of the anomaly. In connection with the clinically observed fact that the disturbances have a strong tendency to spontaneous cure, attention was directed in the first place to retardations owing to which the physiologic building up and extension of the central reflex pathways were interrupted for a shorter or longer time.

As already remarked, I was able to ascertain and confirm the occurrence of monocular eye movements in 85 normal babies. Since every baby starts its life with dissociated eye movements, it seemed obvious to conclude that every one of us is born with a potential squint, that a junction of the two eyes is established by the gradually developing optomotor reflexes, and hence that the appearance or nonappearance of this squint will depend on whether the development of these optomotor reflexes is disturbed or undisturbed. It is obvious that an hereditary factor must also be connected with these developmental disturbances. This view is also excellently compatible with the single dominant hereditary transmission of squint, as ascertained by Waardenburg (1943).

In considering the normal development of the reflexes we have seen how this cortical binocular junction is established.

If, however, the establishment of this binocular junction is impeded by one cause or another, the original dissociated state of the eyes will persist and each eye will direct itself separately according to the resultant of the forces acting on it. If this leads to a monocularly asymmetric gaze tonus, orthophorization will not be achieved.

In the examination of young children with convergent strabismus, the occurrence of dissociated ocular movements could be demonstrated by illumination of the temporal half of the retina. It was found that the adduction innervation predominated over the conjugated and abduction innervations.

These predominating adduction reflexes give a predominance of adduction tonus and to this the characteristic position of the eyes in convergent strabismus must be ascribed (primary squint).

As a direct consequence of this nonparallel position of the eyes, which apparently cannot be corrected by the fusion reflexes, the cortical junction of the homonymous retinal halves cannot take place in the normal manner, so that the possibility of normal binocular vision is excluded.

As a result of this we see amblyopia, suppression, and abnormal junctions (abnormal correspondence).

If, at a somewhat older age, a certain degree of association between accommodation and convergence has formed, an existing tendency to convergent strabismus in hypermetropes will easily become a manifest strabismus. An already achieved (labile) junction may be lost again in this manner (secondary squint).

The now reliably established fact that squint starts during the first year of life in more than half the cases has deprived the fusion and the refraction theories of their basis. In connection with the anatomic structure of the image-forming organs, the ciliary muscle and the retina, on the one hand, and the stage of development of the central fiber tracts and more especially the associative and cortical representatives of the retinal elements, on the other hand, at this early postnatal stage, it is extremely unlikely that fusion and refraction could count as etiologic factors in this period.

The theories of peripheral causes (muscle lengths and mechanical obstacles) are no longer tenable in the light of modern muscular physiology. With regard to the innervation theory of Duane and others I should like to remark:

The innervation theory ascribes convergent strabismus to an excessive convergence tonus which is believed to become manifest owing to the failure of inhibitory cortical influences on a subcortical convergence center* to appear. This explanation, however, is based on two unproved premises:

1. That a subcortical convergence center is already present at birth. The presence of a subcortical convergence center at birth has never been demonstrated. The clinical observation that a convergence reaction cannot be elicited before the age of three months argues against it.

2. That this center derives its tonus from nonoptical reflexes. The origin of these nonoptical stimuli has never been stated. Convergence is a phylogenetically young reflex, so that it is, a priori, unlikely that the convergence center would derive its tonus from subcortical stimuli.

That amblyopia cannot be the cause of strabismus is proved by the frequent spontaneous cures in which the position of the eyes becomes parallel while amblyopia is present and still persists afterward. In accordance with the manner of its occurrence, amblyopia is the consequence of an insufficient development and training of the central monocular reflexes, as a result of which not only the visual acuity—which is higher the more finely the monocular impulses are graduated—often remains lower than normal but also the normal development of the refraction (emmetropization—Straub, 1909, 1910, 1915) is delayed (Stenström, 1950) or prevented. The large percentage of hypermetropes among strabismus patients can be accounted for in this way.

Summing up I may say that the following arguments can be presented for the correctness of the reflex theory:

1. The age at which the affection begins.
2. The dissociated eye movements.
3. The early and gradual development of the optomotor reflexes (convergence; optokinetic nystagmus).
4. The predominance of the adduction reflexes over the reflexes to conjugated movement and over the abduction reflexes.
5. The simple dominant hereditary transmission.
6. The tendency to spontaneous cure.
7. The delayed emmetropization.

None of the older theories is capable of accounting for the many new facts brought to light by recent investigations.

The reflex theory regards squint as the consequence of a disturbance in the physiologic building up of the optical reflex apparatus which has the task of regulating and ensuring the position and function of the two eyes under all conditions, both in associative relationship and for each eye separately.

Clinical statistical investigation has shown that this disturbance must lie in the monocular optomotor reflexes. On the basis of this developmental disturbance it is possible, by

* Bielschowsky (1931) proposed a similar theory for a subcortical center for vertical divergence, in explanation of alternating hyperphoria and the Magendie-Hertwig syndrome.

means of the reflex theory, to give a very satisfactory explanation of the strabismus syndrome in all its details.

B. Alternating hyperphoria

Horizontal squint is very frequently accompanied by vertical position disturbances of the eyes. Among the commonest of these is alternating hyperphoria. The characteristic feature of this anomaly is that when one eye is covered it turns upward.

In a precise and thorough investigation of 113 cases, Crone (1952) found that the phenomena of alternating hyperphoria were practically always associated with a number of other anomalies and this led him to regard the whole complex as a syndrome, in which the alternating hyperphoria was the central, dominant factor. This syndrome includes the following:

1. Upward turning of the nonfixating or covered eye.
2. Strabismus.
3. Hyperphoria in sideways direction of gaze.
4. Rotatory pendular nystagmus.
5. Latent nystagmus with the fast phase in the direction of the uncovered eye.
6. Homonymous rolling of the eyes in the direction of the covered eye.

All these considerations led to the conviction that the syndrome of alternating hyperphoria must be ascribed to a defective development of the monocular optomotor stimuli from the lower nasal quadrant of the retina. As a result of this the fixating eye has a tendency to deorsumduction, adduction, and endorotation. As soon as one eye is covered, these tendencies disappear as far as the covered eye is concerned and this eye takes a higher position with abduction and exorotation. But there is more than this:

The monocular tendencies of the fixating eye are corrected as far as possible by a voluntary adjusting movement. Voluntary adjusting movements are always conjugated innervations. If these conjugated corrective innervations are normally produced, the hyperphoria on occlusion of one eye will not be changed by sursumversion. The chance is, however, that the impulses to conjugated movement from the lower nasal quadrant are also too weak, so that the impulse to sursumversion will have to be supplied chiefly by the temporal lower quadrant. If this is so, an impulse to sursumversion will, then, at the same time, give an impulse to lateroversion in the direction of the covered eye and an impulse to homonymous rolling in the direction of the covered eye. In this way the adduction tendency of the fixating eye is still further strengthened and this tendency has to be repeatedly annulled by an adjusting impulse in the opposite direction. This accounts for the latent nystagmus.

And now a few words about the rolling of the eyes. From the investigations of Noji (1929) and of van der Waals and Roelofs (1938), who showed that parallel rolling of the eyes could be evoked by rotating contours about the line of gaze, and from the investigation of Mesker (1950, 1953), who showed that in this the influence of vertical contours strongly predominates, it appears that the adjusting reflex has as a subsidiary task the placing of vertical contours in the vertical meridian of the retina. From this it follows that impulses to rolling to the right must originate from the right upper and left lower retinal quadrants and impulses to left rolling from the left upper and right lower quadrants.

If, now, the stimuli from the lower nasal retinal quadrant are insufficient, so that a tendency to deorsumduction and endorotation occurs, this implies a too strong tonic innervation of the superior oblique muscle and a strabismus sursoadductorius is to be expected.

In the course of time it is possible for the phenomena to be abolished by a corrective innervation, which must consist chiefly in an accentuated innervation of the oblique in-

ferior and a relaxation of the oblique superior. In divergent strabismus, the optomotor reflexes from the temporal lower quadrant are also less strongly developed and a hyperfunction of the inferior oblique muscle is less likely. This is why no strabismus sursoadductorius is seen with divergent strabismus.

Crone's theory, with which I entirely agree, not only explains the whole complex of phenomena of alternating hyperphoria in a satisfactory manner, but is also supported by the biologic considerations that the optical stimuli acting on the temporal halves of the retinas are in general much more important than those reaching the lower halves.

From these observations and considerations it appears that the disturbed reflexes develop chiefly from the two nasal and the two lower quadrants. The disturbance can affect both the monocular and the conjugated reflexes.

III. Disturbances in the development of the conjugated optomotor reflexes

Among the most important affections that may be regarded as a consequence of disturbances in the conjugated optomotor reflexes are:

A. Pendular nystagmus.

B. Latent nystagmus.

In a recent investigation, Roelofs and Keiner have gathered together numerous facts which give very strong support to this theory. This investigation comprised 55 patients, 42 with latent nystagmus and 13 with pendular nystagmus. Careful attention was paid in these cases not only to the nature and type of the nystagmus but also to the presence of other optomotor disturbances, such as strabismus and alternating hyperphoria, while the binocular vision, the nystagmus with different directions of gaze, and finally the reaction to optokinetic stimulation were also examined.

For a proper understanding of nystagmus, which obviously derives from a disturbed fixation mechanism of the eyes, it is necessary to know what factors normally regulate and determine the position of the eyes in the orbits and in space and how the eyes are then held in the position once assumed.

With the aid of the "innervation tonus" theory formulated by Roelofs in 1936 and since then repeatedly tested by investigation by him and others, it is possible to give a satisfactory explanation of the position and fixation of the eyes under both physiologic and pathologic conditions. The problems of optical localization have also found a solution with the help of this theory (Mesker, 1953).

From the tonus of the ocular muscles it can be deduced that the co-ordination centers for the eye movements are in a continuous state of excitation. This continuous excitation state, which is maintained partly autonomically but certainly for the greater part in a reflex manner by all kinds of peripheral stimuli of nonoptical nature, is called by Roelofs the innervation tonus or, where movements of gaze are concerned, the gaze tonus.

The nonoptical gaze tonus, which is formed chiefly by vestibular and musculosensory proprioceptive stimuli, will for the moment be left out of consideration here.

The optical gaze tonus comprises the light tonus and the fixation tonus. The light tonus is the tension pattern that is provided by the retina under the influence of the originally monocular optomotor impulses emanating from each retinal element. The light tonus, as the resultant of all these impulses, will strive to keep the eye in its neutral position in the orbit.

The conjugated optomotor reflexes, on the other hand, will tend, by virtue of their origin, to keep the eyes at rest with respect to the external world, that is, they will strive to fix the image of the external world on the retina. Any displacement of this image over the retina will call the reflexes into action. Therefore, they are called optical fixation reflexes and they can—in contradiction of the opinion expressed by Kestenbaum

(1921)—originate from any part of the retina.

As the eyes are never still, the fixation reflexes too must be perpetually in action. They thus maintain a tension pattern that contributes to the elevation of the gaze tonus and is called a fixation tonus. Both the monocular and the conjugated optomotor reflexes thus contribute to the optical gaze tonus.

The gaze tonus can be altered both qualitatively and quantitatively. A qualitative alteration gives a change in the direction of gaze and a quantitative modification gives a change in the muscle tonus. The gaze tonus and the optomotor stimuli that make up the tension pattern of the retinal impulses form the basis of the physiologic correlate of the optical localization and thus also of the visual acuity (Roelofs, 1935; Mesker, 1953). The mutual tension engendered by two points which impinge upon the retina at different places can be regarded as the physiologic correlate of the apparent distance between these points, that is, of the exocentric optical localization.

As the visual acuity is nothing but relative exocentric localization, this will be the greater the more sharply the motor impulses are differentiated.

The tension between the gaze tonus and the optomotor impulse to adjusting movement forms the physiologic correlate of the egocentric optical localization. What applies to the exocentric and egocentric localization applies also to depth localization. Here the tension between two convergence impulses is the physiologic correlate of depth perception.

According to the innervation tonus theory as already outlined, the position of the eyes will be dynamically governed under the influence of the tonus of the right and the left co-ordination center, while they will be fixed in the intentional position by the fixation reflexes. All factors which alter the gaze tonus will therefore inevitably be expressed in the position and/or the fixation of the eyes. As is shown by the nystagmus of the blind, the optical components of the gaze tonus (light tonus and fixation tonus) are indispensable to keep the eyes at rest.

Asymmetries of the gaze tonus may be caused either by its nonoptical or its optical component. The nonoptical reflexes, being phylogenetically older, will presumably be less vulnerable. Disturbances of the optical gaze tonus, however, are frequent, as clinical experience shows. An asymmetry of the optical gaze tonus can occur in two ways:

In the first place, it is possible that although the stimuli from either eye do not maintain a predominant tonic innervation to right turning or left turning, yet the stimuli from one eye give a stronger tonic innervation than those from the other eye. This can be due to the monocular optomotor reflexes (unilateral pendular nystagmus) or to the conjugated optomotor reflexes (nystagmus of different intensities in monocular vision).

In the second place, the asymmetry may be such that the stimuli emanating from each of the two eyes give an unequal tonic innervation to right and left for turning. This again can be due to the monocular optomotor reflexes (various kinds of strabismus) or to the conjugated optomotor reflexes (latent nystagmus).

Pendular nystagmus will appear especially in cases where the optical fixation reflexes are not sufficiently able to inhibit involuntary movements and to build up the fixation tonus. A defective development of the monocular optomotor reflexes may in some cases promote the occurrence of pendular nystagmus. Latent nystagmus is considered always due to an insufficient fixation tonus. This deficient fixation tonus is ascribed to a disturbance in the development of the conjugated optomotor reflexes. In practically all cases evidence is also found of a disturbance in the development of the monocular optomotor reflexes, as shown by the presence of strabismus and by the fusion amplitude, visual acuity, and binocular perception.

In order to ascertain the presence of disturbances in function of the optomotor reflexes in my nystagmus patients, I made use of (a) examination of the nystagmus on looking sideways and (b) the reaction to optokinetic stimulation with monocular and binocular vision.

The occurrence of a terminal-position nystagmus points to a relative or absolute deficiency of fixation tonus, while a weak or absent reaction to optokinetic stimulation, or an inverse type, is indubitable evidence of a serious disturbance of the mechanism of the fixation reflexes.

As a consequence of my theory, it follows that a normal and complete development of the monocular optomotor reflexes is necessary for a normal development of the binocular junction, fusion amplitude, binocular depth perception, and visual acuity. Careful attention was also paid to these points in the examination of my patients. I shall now discuss the results of my investigation, first of the cases with pendular nystagmus and then those with latent nystagmus.

A. Pendular nystagmus

Of 13 patients with pendular nystagmus, only three had no terminal-position nystagmus and no disturbance of their optokinetic reaction. Their fixation reflexes, thus, functioned normally, so that I was forced to conclude that they had a disturbance in the development of the monocular optomotor reflexes. In the other 10, who did show a terminal-position nystagmus, it was found that optokinetic stimulation with either monocular or binocular vision was either totally without effect ("optische Drehstarre"), or gave rise to an inverse type. It was clear in all these cases that the pendular nystagmus was caused by a disturbance in the development of the conjugated optical fixation reflexes.

Ter Braak (1936) and Ten Doesschate (1952) have shown experimentally that the absence of fixation reflexes gives rise to nystagmus. Ter Braak stimulated one eye of a rabbit optokinetically and used the other eye for registration. If stationary contours were also visible to the stimulated eye, no nystagmus occurred. When the stimulated eye was immobilized, the other eye showed nystagmus. The explanation is obvious: Owing to the immobilization, the images of the stationary objects could not undergo small displacements over the retina, so that the fixation tonus was not established and nystagmus appeared.

Ten Doesschate continued an image of a source of light as accurately as possible at the center of rotation of the eye, so that the dispersion image of the pupil could not move over the retina when the eye moved. Thus the fixation reflexes were not evoked. When one of the entopic structures visible in the dispersion image was fixated, a very regular pendular nystagmus ensued. He also succeeded in evoking a similar pendular nystagmus with the aid of after-images in a number of persons. A further important point was that nystagmus was evoked by the fixation of entoptic structures, that is, by optomotor stimuli.

The great significance of the fixation reflexes evoked by displacement of light stimuli over the retina, whereby a pendular nystagmus is prevented, is well demonstrated by Ten Doesschate's experiment.

As regards the cause of the disturbances, the influence of peripheral factors such as maculae corneae, congenital cataract, chorioretinitis centralis, albinism, and total color blindness is strongly in evidence in the cases of pendular nystagmus. These will undoubtedly interfere with the normal development of the reflexes. Nevertheless, it does not follow that the point of attack is solely in the retina. It is probable that the cortical representatives of the disturbed retinal elements will also have failed to develop normally, so that their normal junctions will be formed only defectively or not at all. Thus here again the disturbance may be a

central one, while the peripheral anomalies need only be regarded as contributory factors.

B. Latent nystagmus

By latent nystagmus we understand a nystagmus that appears—or at any rate becomes greatly accentuated—only when one eye is occluded or when the light intensity or the sharpness of the image for one eye is greatly reduced.

As a rule latent nystagmus is accompanied by all kinds of complications such as ocular malformations, various types of strabismus, impaired visual acuity, and other disturbances of function, so that the clinical picture is highly variable. Also included under the heading of latent nystagmus are the cases of jerking nystagmus which may be seen in one-eyed persons when the remaining eye is occluded, this nystagmus having its fast phase in the direction of the blind or missing eye.

As in the cases of pendular nystagmus, my 42 patients with latent nystagmus were also examined by means of the nystagmus on looking sideways and the optokinetic nystagmus in order to ascertain the state of development of their optomotor reflexes, both with monocular and with binocular vision. Here again these reactions proved to be dependent on the degree of developmental disturbance and on the presence or absence of symmetry in the disturbances of the optomotor reactions for the two eyes. On the basis of symmetry or asymmetry of these disturbances I divided my cases into three groups, as follows:

Group I. Cases in which the innervation tonus had developed more or less symmetrically.

Group II. Cases in which the nonoptical gaze tonus had developed in a balanced manner but the optical tonus had not.

Group III. Cases in which both the nonoptical and the optical tonus had developed asymmetrically.

In Group I, there were no differences on looking with both eyes to the right and to the left. In Groups II and III, too, there was still a relatively large number of patients who showed symmetric phenomena in binocular laterally directed gaze. In this connection it should be remarked that the gaze tonus in the horizontal plane is the resultant of components for right and left turning. It is possible for these resultants to balance each other although the components may differ in the two eyes.

With monocular vision, the state of affairs was quite different. In practically all cases the jerking nystagmus on looking to the temporal side was found to be the stronger. In some cases of Group III, however, this predominance was compensated by a nonoptical fixation tonus in the opposite direction. The asymmetry in the nonoptical gaze tonus was here manifested by the jerking nystagmus that occurred in the dark. The cases of one-eyed persons with latent nystagmus fit well into this group. They show, in addition to a predominance of the optical fixation tonus in the nasal direction, a compensatory predominance of the nonoptical gaze tonus in the temporal direction. As a result of this the eyes may be practically at rest in the light.

On looking nasalward with one eye, very variable reactions occurred. These depended chiefly on the degree of development of the nasally directed fixation tonus in comparison with that of the temporally directed tonus. Group I did not show any difference between right and left eye with temporal and nasal direction of gaze; in Group II, such a difference was frequently seen; and in Group III, it was the rule on account of the asymmetry of the two components.

In my study of optokinetic nystagmus I found in 23 cases, with both eyes open, symmetric or practically symmetric reactions with movement of the contours to the right and the left. In the remainder of the cases there was an asymmetric development of the

tonic innervation. The nature of the reaction was found to vary widely in accordance with the degree of development of the optical fixation reflexes, ranging from a practically normal reaction to a very weak reaction, no reaction or pendular nystagmus and inverse type.

With monocular vision, the reaction to optokinetic stimulation showed in the overwhelming majority of cases a very marked difference between the temporalward and the nasalward optical fixation tonus. It was almost invariably found that the optical fixation reflexes to a displacement of stimuli from temporal to nasal over the retina were less satisfactorily developed than those evoked by a displacement of stimuli from nasal to temporal on the retina. This reaction is so characteristic that in doubtful cases it can serve as proof of the existence of a latent nystagmus. Where the two eyes were unequal it was found that in the better eye the nasalward fixation reflex was better developed, while in some cases both the nasalward and the temporalward fixation reflexes of the better eye had reached a higher level of development (Group II).

In a number of cases of Group III, it appeared that the asymmetry of the optical fixation reflexes was compensated for the better eye by an asymmetry of the nonoptical reflexes. This compensation was the most nearly complete in the seven one-eyed patients. Evidence of an asymmetric nonoptical gaze tonus is provided not only by the jerking nystagmus in the dark but also by the fact that it is not influenced by optokinetic stimulation.

With monocular stimulation there was also a great variety in the nature of the optokinetic reactions, according to the severity of the disturbance.

Both the nystagmus with laterally directed gaze and the reaction to optokinetic stimulation thus showed that in latent nystagmus there is a definite asymmetry of the fixation tonus, this in turn being due to a disturbance in the development of the conjugated optical fixation reflexes.

Various investigators have sought an explanation of latent nystagmus. Of the most important of these we need mention only van der Hoeve (1917), H. Fromaget (1912-1916), Kestenbaum (1921-1925), Roelofs (1928), and Ohm (1942). Van der Hoeve and Fromaget consider a labile equilibrium of the co-ordination centers to be the primary cause. Kestenbaum postulates a disturbance in the homonymous fixation reflexes evoked by stimuli from the macula. Ohm seeks the explanation in a disturbance of the vestibular muscle tonus. Roelofs was, at the time in question, of the opinion that the labile equilibrium of the co-ordination centers had resulted from a defective tonic innervation, due chiefly to a disturbance in the development of the musculo-sensory proprioceptive reflexes. The contradictions among the various theories made a new investigation desirable.

The results of the investigation reported here compel the assumption that the primary cause of the nystagmus must be sought in a disturbance in the development of the optomotor reflexes and more especially in the optical fixation reflexes. The recently expressed opinion of Crone (1952) is in agreement with this.

It is not possible, in the present state of knowledge, to say much about the nature of these disturbances and their localization in the optical reflex pathway. No morbid anatomic investigation has, as yet, been carried out. For the time being it is only possible to guess at the nature of the disturbances.

Keiner (1952) suggested the possibility of pre- and postnatal disturbances (myelogenesis retardata) in the development of the central nervous system. Heredity undoubtedly plays an important role. Familial occurrence was also seen among my cases.

As regards the point of action of the disturbances, it appears certain that this must be sought somewhere in the optical reflex pathways. I am of the opinion that an affection of the nucleus of Deiters, as suggested by Ohm, can be excluded. One is inclined to look for the disturbance in that part of the

reflex arc over which the optical impulses reach these co-ordination centers or to point to the area striata with its direct neighborhood in the area parastriata and peristriata (Brodmann's areas 17, 18, and 19). The frequent occurrence of strabismus and the accompanying electroencephalographic anomalies observed might be taken into consideration in this direction.

If we assume that there is an asymmetry in the impulses conveyed along the afferent optical reflex paths, we are justified on the grounds of Roelof's' investigation (1928) in concluding that in latent nystagmus this is not due to a difference in the stimuli from the temporal or the nasal half of the retina. This might also support the hypothesis of a central site of the disturbance.

Only a guess at the anatomic substratum of the anomaly can be hazarded for the present. By analogy with what we believe to be the case in disturbances of the establishment of cortical binocular junction (strabismus) it might be surmised that disturbances in the linkage of the cortical representatives of certain retinal elements exist also in nystagmus, so that instead of the normal two-way traffic between neighboring cortical representatives there is only one-way traffic (latent nystagmus) or no traffic at all (pendular nystagmus). All degrees of transition between these situations are theoretically possible and these were in fact also found in our investigation.

Reasoning along these lines one comes easily to the idea of a disturbance in the formation or consolidation of synapses. One might speak here of an absence of defective development of the cortical monocular junction. If one now surveys the various disturbances in the development of the optomotor reflexes and the clinical pictures which inevitably result from them, one finds that the latter show many points of similarity.

In all cases, the manifestations start at a very early age, usually in the first few months of life. They all have a pronounced hereditary character and very frequently occur in combination. Solitary disturbances are rare; as a rule both the territory of the monocular and that of the conjugated optomotor reflexes are affected, although in varying degrees. Gradual improvement in the disturbances, with transition from a severe disturbance to a less troublesome one (from pendular nystagmus to latent nystagmus) is known to occur (van der Hoeve, 1917; Roelofs and Keiner, 1954) and all kinds of intermediate stages are also possible. In all cases practically the same factors are found to contribute to the disturbance. In all cases, too, there is much evidence that points to a central localization.

All this is in favor of a single common (hereditary) cause of all these disturbances. This implies that the clinical form in which the disturbance will be manifested will depend on the degree to which the monocular or the conjugated optomotor reflexes, or both, have suffered interference with their development. The gradual transition from one clinical picture to another and the spontaneous improvements which are known to occur point rather to a delayed physiologic development (retardation) than to any pathologic process.

Recapitulating we may say that the clinical pitcures produced by disturbances in the development of the optomotor reflexes are the consequence of an insufficient or asymmetric gaze tonus. Both the optical and the non-optical components can contribute to this disturbance. The disturbances of the optical component can be further subdivided into disturbances of the light tonus, based on the monocular optomotor reflexes, and disturbances of the fixation tonus, based on the conjugated optomotor reflexes. In many cases the disturbance will be a combined one, while finally a secondarily disturbed non-optical component may further complicate the picture.

Leaving the latter out of consideration I may say that I have observed the occurrence of pendular nystagmus as a consequence of an insufficient light tonus or fixation tonus, or of both. In these cases the developmental

disturbance was due to a practically complete absence of cortical monocular junction. The consequences of an asymmetric gaze tonus can be manifested in two ways according to the severity of the disturbance. If this is slight, so that there is no pronounced tendency to right or left turning, and the disturbance is based on the monocular optomotor reflexes, a unilateral pendular nystagmus is obtained. If it is based on the conjugated optomotor reflexes, the pendular nystagmus will be unequal in the two eyes when each is tested separately. If the disturbance is more severe, so that there is a pronounced tendency to right or left turning, and the anomaly is based on the monocular reflexes (light tonus) we can expect all kinds of strabismus as a consequence.

If the affection is based on a disturbance in the development of the conjugated optomotor reflexes (fixation tonus), the consequence will be a latent nystagmus (defective cortical monocular junction). In strabismus there exists, as is known, an absence or severe insufficiency of the cortical binocular junction which is the cause of the disturbance of development of the reflexes; while in nystagmus, it must be the cortical monocular junction that is absent or defective. Combinations of disturbances in both the cortical monocular and the cortical binocular junction are not infrequent.

Reasoning along these lines one can reduce the problem of disturbances in the development of the optomotor reflexes to a disturbance in the cortical junction of the representations of the various retinal elements, that is, in the conduction and transmission of impulses in the cortical retina. With a knowledge of the retinal quadrants from which the reflex disturbance is manifested, it is possible to indicate the topographic situation of the disturbed areas in the cortical retina. The morbid anatomic investigation of structure and function will have to be concentrated on these regions, now that clinical studies have given the lead, in order that these considerations may be placed upon a sound factual basis.

The following schema may serve for the judgement and interpretation of observed disturbances of the optomotor reflexes:

I. Monocular optomotor reflexes

a. Slight disturbances: Insufficient cortical binocular junction as shown by the visual acuity, fusion amplitude, and binocular depth perception.

b. Severe disturbances: Absence of normal cortical binocular junction, manifested by the various forms of strabismus.

II. Conjugated optomotor reflexes

a. Slight disturbances: Insufficient cortical monocular junction. Tendency to slight pendular nystagmus.

b. More severe disturbances: Cortical monocular junction developed in only one direction. Latent nystagmus.

c. Very severe disturbances: Cortical monocular junction absent. Pendular nystagmus.

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Discussion

Francis Heed Adler (Philadelphia): In accepting the invitation to discuss Dr. Keiner's manuscript I had counted heavily on having an opportunity of going over a number of points with him which were not clear to me. His illness prevented our meeting and his tragic death on October 2nd, has now made it impossible for me to do justice to his important contribution.

Based on his monograph, which appeared two years ago, and this manuscript, I would like to outline what I believe to be the essential features of Keiner's theory. In essence, he agrees that the reflex control of ocular movements is maintained by two more or less separate mechanisms:

1. That which I and other authors refer to as the postural reflexes, which are evoked by non-optical stimuli. These, he believes, are manifested in two forms; one is a monocular reflex evoked by proprioceptive impulses coming from the ocular muscles and their fascia, and the other comprises conjugate compensatory reflexes evoked by vestibular and musculo-sensory stimuli from the labyrinths and neck muscles.

2. The reflex eye movements which are evoked by optical stimuli, which most of us refer to as the optomotor reflexes. Keiner believes that these optomotor reflexes produce their effects by being grafted on to the more primitive postural reflexes. He states that they appear in two forms: (a) a monocular optomotor reflex grafted on to proprioceptive reflex pathways, and (b) conjugate optomotor reflexes grafted on to vestibular reflex pathways.

As far as I have been able to find, there is no experimental proof for this conception, and I would like to point out that although we now know the eye muscles of man do have specialized nerve endings which are probably proprioceptive in nature, we are still not in agreement as to how important proprioception is in the control of ocular movements.

Keiner tries to show that the more primitive reflexes which were originally monocular in effect gradually evolved into binocular eye movements. In his own words:

"The repeated coincidence of identical monocular and conjugate adjusting reflexes in both eyes, as evoked by the predominance of a given stimulus from the outside world, will give rise to ever repeated simultaneous stimulation of corresponding retinal elements and will lead to the formation of a functional junction between the cortical representations of these retinal elements, and finally between the entire homonymous retinal halves of the two eyes. This new motor link between the two eyes at the cortical level, which in man has its anatomic substratum in the semidecussation, we call the cortical binocular junction (Keiner 1951) to distinguish it from the subcortical junction via the conjugate reflex pathways. On the basis of this junction, identical adjusting reflexes will combine to give a single adjustment innervation; *the impulse to an originally monocular eye movement has thus become an impulse to binocular eye movement,** owing to the fact that when a certain retinal element is stimulated, not only its own cortical representative, but also the cortical representative of one of the corresponding retinal elements will emit a motor impulse."

There is nothing in this which we cannot accept, although it seems a rather novel way of putting an old idea. In other words, if I give an optomotor impulse to my right eye while the left eye is closed or shielded from the stimulus, both eyes will automatically turn to the object of regard. However, Keiner amplifies this idea to the point where he steps pretty deep into uncharted waters. He says:

"It is thus the cortical binocular junction that creates the possibility of a common innervation impulse, and hence of a harmonious distribution of the impulses over the two eyes. Where such junction is absent (strabismus) Hering's law is also not valid."

I take this to mean that Hering's law is not valid in cases of strabismus, and I feel there is good evidence that this statement is untrue. I am in agreement with Keiner when he states that the tonic reflexes which are chiefly concerned with maintaining the position of the eyes are of great importance in both physiology and pathology in cases of squint, and that the "pathology of the optomotor reflexes occurs to a considerable extent in the field of the tonic innervations." In other words, that strabismus has to do with some upset in the tonic reflexes, and, as I have stressed elsewhere, in the tonic reflexes for vergences. These tonic reflexes are postural reflexes of the eyes in the sense in which the term was used by Magnus.

I would like to know the evidence for the statement Dr. Keiner makes as follows:

"Where the two eyes are unequal, it is possible to find that in the better or preferred eye, the reflexes have developed better or reached a further stage than in the poorer eye."

A further statement on which much of his reasoning depends is not quite clear to me:

"Our nystagmus studies have brought out the fact that for a normal functioning of the reflex apparatus it is equally necessary that a cortical monocular junction of the cortical representatives of the retinal elements be built up."

Just what does this mean?

Following this, the provocative and all-important statement is made:

"The problem of ocular imbalance is to a great extent the problem of the central junction."

I am sure Dr. Keiner is in agreement with me that the problem of strabismus is the problem of heterophoria. He and I are therefore both interested in the site of the disturbance which creates the heterophoria. He does say that, ". . . retardations in the normal building up of tracts and synapses

* Italics mine.

underlie the disturbances, and that it is only rarely necessary to consider the action of a pathologic agent." He believes that the evidence supports the idea that these affections must be sought for in the occipital lobe. He states that he and Crone have succeeded in showing that strabismus and alternating hyperphoria must have their origin in an imbalance of the monocular optomotor reflexes.

I agree that a great many cases of strabismus start at birth or in the first few months, but not all. I do not believe that this fact in any way disproves the theory of refractive errors being the cause of some cases of strabismus. Keiner states that in the examination of young children with convergent strabismus, associated ocular movements could be demonstrated by illumination of the temporal half of the retina. He found that in these cases the adduction innervation predominated over the conjugated and abduction innervation. Did he test this in normal children also? We know that in the normal child what we call tonic convergence is excessive. I would suspect that he would find this in normal children as well as in children with convergent strabismus. I still believe that one form of strabismus is definitely due to refractive errors, as Donders originally stated, but I agree that this group of cases is comparatively small compared to the total group of strabismus patients. I have always fought for the belief that strabismus was not a single disease entity, but was merely a sign that something had disturbed the mechanism normally associating the eyes. I still believe that strabismus is a disturbance of ocular motility due to a number of separate and unrelated pathologic processes. The idea that some of the patients whose strabismus develops at birth are due to delayed myelination is intriguing, but I believe not yet proved. This paper is very thought-provoking, and it is most regrettable that its author could not live to carry on his highly original, experimental approach to the subject.

CORNEAL THICKNESS*

Its measurement and changes

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Uppsala, Sweden

The famous French surgeon Petit seems, in 1723, to have been the first to perform scientific measurements of the thickness of the cornea of the human eye. He found a thickness of about 0.4 mm. which is surprisingly low with regard to the values given by later examiners who also used enucleated eyes of cadavers. These values are between 0.7 and 1.0 mm. It is rather astonishing to find that these values are often still used in textbooks and papers mentioning the thickness of the cornea.

As we all know, the cornea has a very great swelling capacity and very soon after death loses some of its transparency on account of swelling. It is very likely, therefore, that the measurements on dead eyes give too high values and also varying results. What we are interested in knowing is the thickness of the cornea of the *living* eye, and in the last 75 years several methods have been developed for its measurement.

The physiologist, Blix, at Uppsala, in 1880, was the first to invent a method for such a measurement. His ophthalmometer consisted of two horizontal microscope tubes with optical systems of equal power, the directions of which converged at an angle of about 40 degrees to a point in front of the tubes (fig. 1). In one of these tubes there was a well-illuminated diaphragm so adjusted that its image was situated at the point of intersection of the axes of the microscopes. The tubes were movable symmetrically along their axes and also, without alteration of their position relative to one another, along the line bisecting the angle between them. When the distance between two reflecting surfaces of an optical system (as the anterior and the posterior surfaces of the cornea) was to be measured, the latter movement was executed, and the apparatus was first adjusted so that the il-

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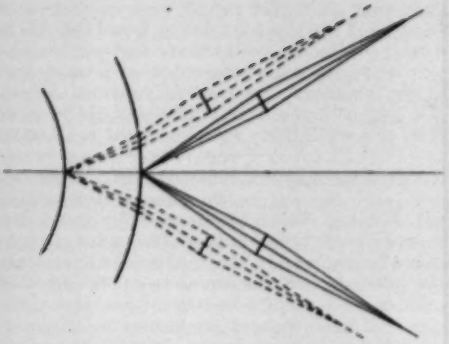

Fig. 1 (von Bahr). Diagram showing optical system of the Blix ophthalmometer.

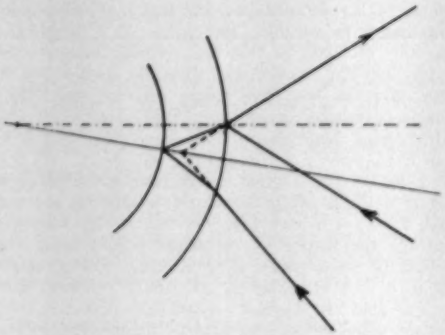

Fig. 2 (von Bahr). Diagram showing optical system of Gullstrand's apparatus.

luminated image from the one microscope by reflection from the anterior corneal surface was seen at the corresponding place in the other microscope. After that the same adjustment was made for reflection at the posterior surface. The difference in position gave the apparent thickness of the cornea and the real thickness was easily calculated when the radius of curvature of the anterior surface and the refractive index of the cornea were known.

Gullstrand also used the reflections from the two corneal surfaces for his measurements (fig. 2). By a special device consistting of two lamps, with vertical slits placed immediately above and below a telescope and a movable fixation spot, he at first determined the perpendicular that is common to both the surfaces. Then lamps with aligned vertical slits on one side and a telescope on the other were placed symmetrically 25 degrees from this perpendicular, so that the slits were seen reflected by the posterior corneal surface. A movable weak linear light source was then adjusted in such a way that its reflection from the anterior surface was seen in line with the reflections described, from the posterior surface. The angle between the line from this linear source of light to the cornea and the common perpendicular to the corneal surfaces was measured. These data and the values for the radius of curvature of the corneal and the refractive index of the corneal tissue made it possible to calculate the corneal thickness. The set up of apparatus was rather complicated and was used only in two cases. Tscherning followed the same principle.

The invention of the corneal microscope and Gullstrand's slitlamp has given other possibilities for such measurements. According to Hartinger, Ulbrich's measurement drum can be used for this purpose. The corneal microscope is focused on the anterior surface as well as, subsequently, on the posterior one. This may be facilitated by a beam of light from the slitlamp passing through the part of cornea to be measured. The difference in the positions is read on the drum and gives the apparent thickness directly. Fincham and probably also Sobanski seem to have used this technique.

Another use of the slitlamp has been worked out by Koby and Juillerat. The corneal microscope (fig. 3) was placed with its axis parallel with the approximate optical axis of the eye and the slitlamp beam of light with an angle of 45 degrees to this. The apparent length of the optical section through the cornea by this beam was measured with an eyepiece micrometer in the corneal microscope. The real thickness of the cornea is calculated by aid of formulas based on the assumption that the corneal surfaces are concentric.

Of the methods described, that of Gullstrand is the most accurate one but it is also the most complicated one to use and therefore not convenient for routine measurements. Out of the other ones Blix's method is best from theoretical point of view, but all of them have the disadvantage that the measurement requires absolute fixation of the eye. No movement of the eye should be allowed between the adjustments or readings pertaining to the anterior and posterior surfaces respectively. Even a very small movement can cause a fairly large error when such a small distance as the corneal thickness is measured.

In order to avoid the theoretic and practical objections to the methods described I have constructed the following apparatus (fig. 4). It is based on the same principle as Blix's ophthalmometer but the adjustment to both the corneal surfaces is done simultaneously. This is brought about by two plane glass laminæ which are symmetrically movable about vertical axes in front of the optical systems of the devices for illumination and observations in such a way that only rays of the lower halves of these systems have to pass through the laminæ. In the zero position both the laminæ are perpendicular to the rays and do not change the path of these, but when they are turned the rays passing the laminæ will be displaced into a parallel path. If the axis of the apparatus coincides with the perpendicular common to both the surfaces of the cornea, the displacement can be made to such an extent that the reflection from the anterior and

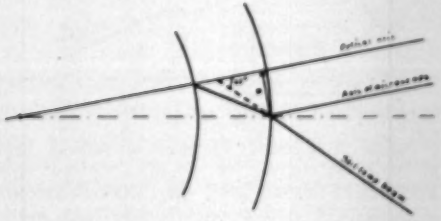

Fig. 3 (von Bahr). Diagram showing the use of the slitlamp as worked out by Koby and Juillerat.

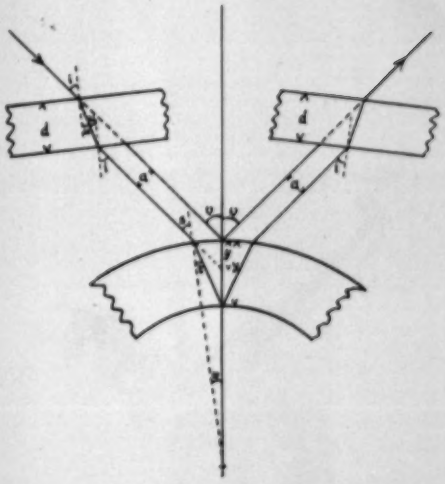

Fig. 4 (von Bahr). Diagram showing the optical system of the apparatus constructed by von Bahr.

the reflection from the posterior surface will be seen in the same place, or, in practice, on the same straight line. The turning of the laminæ thus stands in some proportion to the thickness of the cornea.

The thickness is easily calculated from the angle of revolution, the thickness of the glass laminæ, the index of refraction of the glass, and the cornea and the corneal radius.

In the apparatus (figs. 5 and 6) I used an old slitlamp and an old corneal microscope with one objective. The instrument should be adjusted to the perpendicular common to both the surfaces. As the determination of this perpendicular requires a special apparatus I have used the perpendicular through the center of the pupil as an axis instead. There is some evidence that this introduces an error in the measurement, but this error is very small.

The standard error of a single reading was found to be ± 0.013 mm. in measurement of the cornea of a living man. When the mean of three readings was used as a single determination, its standard error was ± 0.0077 mm. In measurements on narcotized rabbits I found the same standard error at ± 0.009 mm., that is ± 2.3 percent

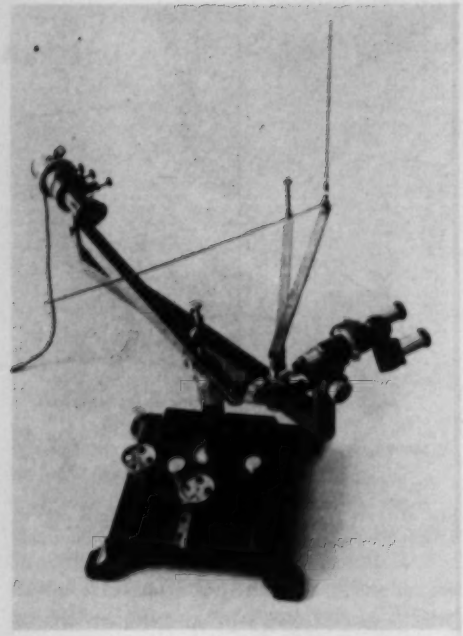

Fig. 5 (von Bahr). The apparatus.

of the normal thickness of the rabbit cornea.

Thus the method is fairly accurate and I have found it rather easy to handle. But it has some drawbacks. There are eight images of the slit formed by the optical system and this might be a little confusing, though it is generally easy to know which of the images is to be aligned. A more serious disadvantage is that the reflex image from the posterior is much weaker in brightness and when the corneal substance is rather opaque it will be impossible to see. It is also impossible to get good reflex images when the corneal surfaces are not quite smooth.

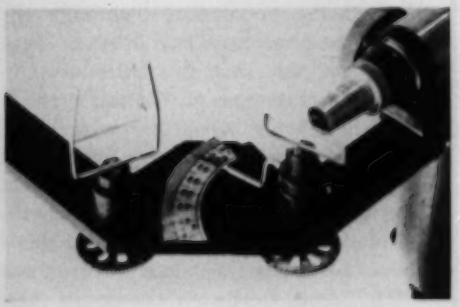

Fig. 6 (von Bahr). Another view of the apparatus.

Maurice and Giardini therefore have simplified the apparatus (fig. 7). They use a perspex plate in the illuminating beam from the slitlamp only. This plate is thicker than the glass plates in my apparatus and it is transversed by a horizontal cut covered by a thin colored strip of celluloid. When the arms of the slitlamp and microscope are fixed with a definite angle, 50 degrees, and the slitlamp beam focused to about its apex, the apparatus can be adjusted so that the white reflex from the posterior surface and the colored one from the anterior surface are both seen in the microscope at the same time. Their brightness is of about the same degree. By rotation of the perspex plate they are aligned and the angle of rotation gives a measure of the corneal thickness. For the calculation of the real thickness it is assumed that the corneal surfaces are concentric, and the calibration is performed by measuring the thickness of the walls of glass and celluloid cylinders.

The standard deviation for a measurement

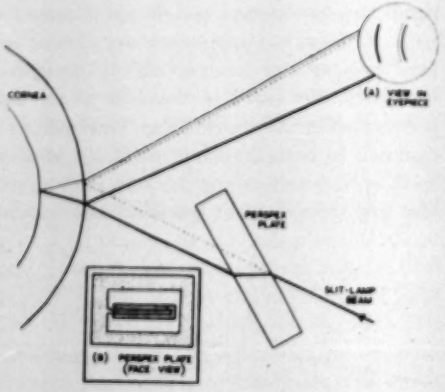

Fig. 7 (von Bahr). Diagram of path of rays, slitlamp lens omitted for simplicity. Colored light indicated by broken lines. (A) View in eyepiece with epithelial and endothelial reflections nearly in alignment. (B) Face-on appearance of perspex plate with celluloid covering saw-cut.

TABLE 1

MEASUREMENTS OF LIVING CORNEAS

Name	Date	Number of Eyes	Corneal Thickness		
			Extreme Limits	Mean	σ
Blix	1880	10	(0.482)0.506–0.576(0.668)	0.541	
Gullstrand	1909	2	0.46 –0.51		
Koby	1928	20	0.466–0.703	0.583	
Fincham	1930	12	0.48 –0.59	0.53	
Sobański	1934	20	0.40 –0.67	0.53	
von Bahr	1948	224	0.46 –0.67	0.565	±0.035
Maurice & Giardini	1951	44		0.507	±0.028
Cook & Langham	1953	10		0.536	±0.04

with this instrument is said to be ± 0.011 mm.

Of the methods described that of Gullstrand is the most accurate one and fulfills all theoretical requirements, but it is too complicated for routine work and investigations where numerous measurements are needed. My own method is free from most of the common theoretic objections to the methods of measurements and has proved useful in some investigations. Maurice and Giardini's method seems to be more easy to handle and to be of about the same accuracy. The objection that it is based on the assumption that the corneal surfaces are concentric does not prevent it from having practical value in comparing measurements on the same spot of the cornea at various conditions and especially in measurements of the rabbit cornea where the corneal surfaces probably are practically concentric in a large area.

Why should we measure the thickness of the cornea? First, it is of anatomic interest to know the dimensions of the organs of the body. Every respectable textbook gives values (but it is nowadays often done with very little respect for the modern scientific facts). It has of course also some interest in practical surgical work to know this dimension. The corneal thickness is also of significance in the studies of the optical properties of the eye—and this was the main reason for Blix's and Gullstrand's studies on the matter. But as it has been known that the transparency and the hydration of the cornea are related to each other and that pathologic conditions can alter the thickness of the cornea, measurements of this thickness have been a help in the studies of corneal physiology and pathology and the role of the ocular fluids.

First, I want to discuss the thickness of the healthy cornea in man. Only the measurements on living corneas are worth mentioning nowadays (table 1).

Blix (1880) measured 10 eyes in eight persons and found values between 0.482 and 0.668 mm. or, if the extreme values which were both obtained in the same person are excluded, between 0.506 and 0.576, with a mean of (0.548) 0.541 mm. Gullstrand (1909) in two eyes found 0.46 and 0.51 mm. Koby (1928) in 20 cases found an average value of 0.583 mm. with variations between 0.466 and 0.703; Fincham (1930) in 12 cases 0.53 with variations between 0.48 and 0.59, Sobanski (1934) in 20 eyes 0.53 mm., with variations from 0.40 to 0.67 mm. All these materials are small but the values agree well even if those of Koby are fairly high. The series are too small to justify a comparison between different groups of persons.

I have examined 224 healthy eyes of 125 persons of different sex and age. The mean for the total of 224 eyes was 0.565 ± 0.0023 mm., = ± 0.0351. Thus the limits of normal variation practically are 0.46 and 0.67 mm. There was no significant difference between the sexes. The mean of the thickness

of 28 corneas from persons above the age of 65 was 0.571 ± 0.0071 mm. and the corresponding figures for 55 corneas of persons below the age of 25 was 0.559 ± 0.0045 mm. The difference, 0.012 ± 0.0048 is not significant. Unfortunately I could not measure the corneas of very small children, which according to the results of anatomic investigations (Petit, Baratz, v. Hippel) are said to be thicker than those of adults.

Generally the thickness seems not to be correlated with the refraction (table 2). But as the extreme cases of ametropia have to be regarded as groups outside the biologically normal group of eyes, I tried to find out if their corneal thickness differed from the others. In eight cases of hyperopia above +3D. the average thickness was 0.565 mm., that is, the same as in the total material. But in 12 cases of myopia more than −4D., the thickness was always lower than this mean. The average thickness in this material of myopics was 0.524 ± 0.0065. The difference from the mean of the total material is − 0.041 ± 0.0668 mm. and is significant. This speaks against the statement given, for example, by Lindner without statistical proof, that the stretching in myopia only occurs in the posterior part of the bulb.

Maurice and Giardini measured the cornea of 44 persons (24 men and 20 women) in ages from 18 to 35 years. They got a mean of 0.507 ± 0.0042 mm., σ = 0.028. There was no significant difference between the sexes. The value was take from the part of the central cornea where it was found smallest.

Cook and Langham (1953) have given a somewhat higher value 0.536 ± 0.04 after measurement of 10 normal eyes.

These values are smaller than mine and the authors discuss the possible reason. As the dispersion was not much greater in my series than in theirs the difference cannot be explained by the fact that I have measured the thickness at the perpendicular to the center of the pupil and they at the part of the cornea which they found thinnest. There may be a systematic error in one or the other. Without a direct comparison between the methods in the same subjects it is not easy to tell its cause.

In pathologic cases the corneas often are thicker than normally. When the increase has reached a certain amount it is evident by the development of folds in the Descemet and also opacification by hydration, but with measurements increase in thickness can often be found without these apparent symptoms. This is common in *keratitis*. In interstitial keratitis Cook and Langham measured an abnormal increase in corneal thickness in all the cases examined. It rose to its peak during the more florid manifestation of the condition and then slowly diminished. The swelling showed a marked tendency to be maximal toward the center, where the thickness sometimes was more than 1.2 mm., that is, more than twice the normal thickness. In cases with corneal vascularization an increase in thickness was always found in association. In all cases the administration of subconjunctival cortisone was followed by a marked decrease in corneal thickness as

TABLE 2

CORNEAL THICKNESS

	Number of Eyes	Mean Thickness (in mm.)	Difference
Men	112	0.565 ± 0.0036	0.001
Women	112	0.564 ± 0.0030	
Persons above 65 yrs.	28	0.571 ± 0.0071	0.012 ± 0.0084
Persons below 25 yrs.	55	0.559 ± 0.0045	
Myopia above 4.0 D	12	0.524 ± 0.0065	−0.041 ± 0.0068
Hyperopia above 3.0 D	8	0.565	

well as in the associated infiltration and vascularization.

In *corrosion* of the corneal surface an increase in thickness can be found which decreases as the healing progresses.

In *iridocyclitis* an increase in corneal thickness is often found by measurement even if the cornea looks unaffected by common methods of examination.

For studying the conditions affecting the corneal thickness more closely it is necessary to turn to experiments. Some can be performed on human eyes. If such an eye is bathed with distilled water for half an hour I have found an increase in thickness of 0.04 to 0.05 mm., and a smaller increase if 0.5-percent solution of sodium chloride was used. At bathing with hypertonic salt solutions I have found a tendency to decrease in thickness, but when the concentration was two percent or more of sodium chloride the solution produced an unpleasant feeling in the eye. For that and other reasons I have performed most of my experiments on rabbits.

The rabbits had been narcotized with Numal intravenously and afterward firmly fixed to a stand which could be moved between certain positions making adjustments of the measuring device possible on the right and on the left eye alternately. Even if this method does not make it possible to reproduce the measurements on exactly the same spot, double determinations have shown that the standard mean error of such a determination with three readings is not more than ± 0.009 mm. As the thickness of the rabbit's cornea is an average 0.40 mm., the standard mean error is only ± 2.3 percent of the normal thickness. In the experiments with bathing of the cornea with different solutions the determinations have been performed on the right and the left eye alternately with an interval of a few minutes. For judging the effect of a certain bathing solution the mean of two successive determinations on each eye has been used. The standard mean error of this mean is ± 1.8 percent and the standard error of the difference between two such means is ± 2.3 percent. On account of this such a difference has to exceed ± 6.9 percent in order to be statistically proved.

I am, of course, fully aware that the values obtained in different states of turgescence of the cornea are not quite correct as absolute values. At the calculation of the real thickness a constant value of the refractive index of the corneal parenchyma has been assumed. But in different states of hydration this index ought to be changed and therefore also the relation between the apparent and the calculated real thickness. For this investigation, however, it is enough to obtain relative values and this source of error can be ignored.

The bathing of the eyes has been performed by keeping test tubes with the solutions to be tested over each eye for a certain time, generally for 10 minutes. Immediately after this the measurements were performed.

In the experiments on man it was evident that hyposmotic solutions brought on an increase in corneal thickness and hyperosmotic solutions a decrease. The same is seen in rabbit's eyes, for example, when the concentration of the solution is 0.5-percent and 2.0-percent sodium chloride respectively (fig. 8). If the variations in concentration are smaller the change in thickness is less marked. Thus the osmotic pressure of a solution in contact with the anterior surface of the cornea has some influence on the corneal thickness. But there is a solution in contact with the posterior surface and this might also be of some significance. It is interesting to see what happens if this solution is eliminated. It can easily be removed and air substituted.

If one compares the thickness of the cornea in such eyes, when air has been substituted for aqueous, with the corneal thickness of normal eyes, it is found to be the same before bathing, at least in my experimental conditions (fig. 9).

If the bathing was performed with a 0.8-

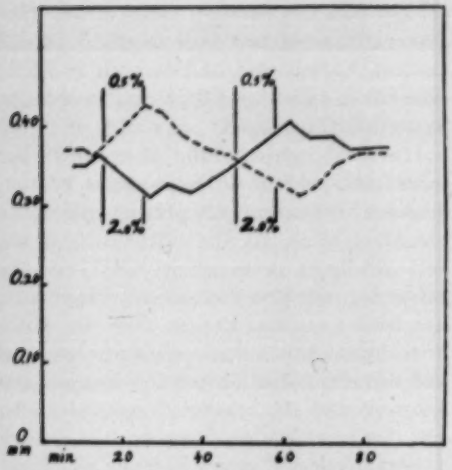

Fig. 8 (von Bahr). Variations in thickness of cornea caused by bathing with 0.5-percent and 2.0-percent NaCl solutions. ———— Right-eye ..... Left eye.

percent solution of sodium chloride the corneal thickness of normal eyes was increased by 6.7 percent as an average, but in air-filled eyes by 21.3 percent.

With 0.9-percent saline no significant change (a decrease of 0.3 percent) was found in the natural eyes but in the air-filled ones an increase of 8.3 percent, which is significant.

With 1.0-percent saline, however, no difference in thickness was found in either kind of eyes, as the differences in thickness before and after bathing were −0.17 percent and +0.08 percent respectively.

With 1.1-percent saline the differences in both kinds of eyes were also very small. They were 2.0 percent and 4.0 percent respectively.

With 1.2-percent saline they were greater as the decreases in thickness were 5.1 percent and 9.7 percent respectively.

With 1.4-percent saline the differences were 4.8 percent and 15.9 (±1.38 percent). The difference is 11.1 ±3.08 and must be regarded as quite significant.

With 1.6-percent solution of sodium chloride the decreases were greater, that is, 9.4 percent and 19.2 percent and with 2.0-percent saline they were even greater, that is, 11.0 percent and 30.0 percent respectively.

These results clearly show that the changes in corneal thickness due to osmotic forces become greater when the aqueous is replaced with air. This applies to the increase as well as to decreases in corneal thickness. It is also apparent that in air-filled eyes changes can appear by bathing with solutions that have no obvious effect on natural eyes. This has been most obvious in the experiments with 0.9-percent saline which solution has not provoked any change of the corneal thickness in the natural eyes but a significant increase of thickness in the air-filled eyes.

Because of these facts the effects of bathing with different solutions, especially when small, are most reliably studied in eyes where the aqueous is replaced with air. Against this it can be held that one is adding an unphysiologic factor to the examinations. As the changes in natural and in air-filled eyes go in the same direction though to a different extent this objection cannot be of any essential significance in this investigation.

In the tests with solutions of sodium chloride of different concentrations it seems most remarkable that a 0.9-percent solution that is isosmotic to blood plasma and tissue fluid produces a swelling of the cornea, thus acting like a hypotonic solution in relation to

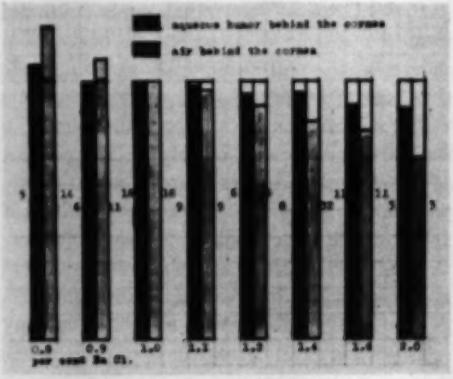

Fig. 9 (von Bahr). Chart of results when air has been substituted for aqueous.

the corneal parenchyma. A solution of 1.0 percent, however, has no effect of that kind while a solution of 1.1 percent shows a slight deturgescent effect. It seems, therefore, that a solution of about 1.0-percent sodium chloride should be regarded as isosmotic with the corneal parenchyma.

But these experiments show more. It has often been stated that, according to Leber's opinion, the intact cornea is not permeable to water. Later Fischer declared that water could pass the cornea from outside into the eye but not from within and out. In experiments on enucleated eyes, however, F. Ridley in 1930 showed that these opinions are not correct. But his results were not generally accepted because of the unphysiologic conditions in the experiments. I was interested in the problem in 1941 and performed some experiments by leading dry air through a chamber covering the cornea and measuring the uptake of water in this air. I found that it was greater when the eyes were intact than when their anterior chambers were filled with air, and concluded that some water could pass through the posterior surface of the cornea to the anterior one, for the possibility of water diffusion from the limbus was always the same.

Cogan and Kinsey in 1942 reported the same processes in isolated corneas.

The present series of experiments show in a more physiologic way in living eyes in situ that water can pass through the cornea in both directions. As the limbal connections are the same in all the experiments there is no reason to believe that the change of water content of the cornea giving the change in thickness should be caused by water going through the limbus. The change in thickness brought on by bathing the anterior surface with solutions of different composition can be either an increase or a decrease which shows that water can pass the anterior surface in both directions. These changes are much greater when there is air behind the posterior surface than when there is aqueous humor. This fact shows that some of the water entering the cornea from in front leaves through the posterior surface and that some of the water leaving through the anterior surface is substituted by water entering from behind. Thus water passes both surfaces in both directions.

The different effect on the corneal thickness of solutions of sodium chloride of different concentrations can be explained by the different osmotic pressure of the solutions. The tissue at the anterior surface of the cornea then must act as a semipermeable membrane permeable to water but not to sodium chloride to the same extent. It is then interesting to see how solutions of other substances act in this respect.

I have chosen to work with solutions isosmotic to a 1.4-percent solution of sodium chloride, which in 10 minutes causes an average decrease in thickness of 15.9 percent ($\sigma = \pm 7.8$ percent). The freezing point depression of this solution is 0.80°, and the solutions used had the same freezing point depression according to Lund, Pentiche, Nielsen, and Pederssen-Bjergaard.

When I used salt-solutions (fig. 10) for bathing the corneal surface the corneal thickness always decreased. The means for the decreases at measurements on two different animals were the following: For 4.0-percent KJ 13.4 percent, for 2.53-percent KNO_3 13 percent, for 3.5-percent KH_2PO_4 19.4 percent, and for 10.3-percent $MgSo_4$ 26.4 percent. Thus the effects were of practically the same magnitude as with the use of an isosmotic solution of sodium chloride, probably somewhat higher with magnesium sulfate.

A 7.7-percent glucose solution is isosmotic with a 1.4-percent sodium chloride solution. After bathing with this solution for 10 minutes I found in eight cases sometimes a slight increase, sometimes a slight decrease in thickness, as an average an increase of +1.8 percent, which means that the solution had no significant effect on the state of turgescence of the cornea. The difference in effect between a 7.7-percent glucose solution and a

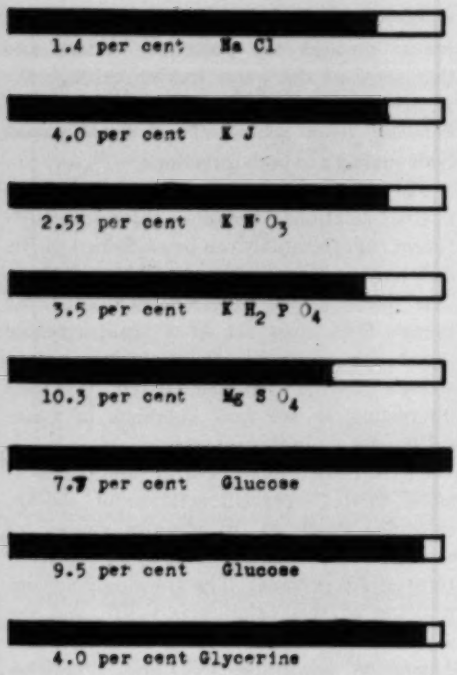

Fig. 10 (von Bahr). Results with salt solutions of various strengths.

1.4-percent sodium chloride solution was 17.7 ± 3.08 percent. After bathing with a more concentrated glucose solution, 9.5 percent, there was, however, a small decrease in thickness of 5.1 percent (three cases).

Also some other solutions of nonelectrolytes isosmotic with the former ones were tested. A 4.0-percent solution of glycerine was used. The measurements of the effect showed a small increase in corneal thickness but the mean from three cases was 4.9 percent only which, with regard to the errors of the method, hardly can be taken as a reliable effect.

A solution of 1.97-percent ethyl alcohol in two cases gave a small increase in thickness, as an average 7.4 percent.

It is very remarkable that the osmotic effect of electrolytes such as sodium chloride is so strong. But this is in good agreement with the findings of Cogan, Hirsch, and Kinsey (1944) on isolated corneas. The effect of glucose and glycerin solutions is much smaller though the molecular size of these substances is greater. This shows that other physiochemical properties must be of importance. This is still more apparent when more unphysiologic solutions are used, for example, ethyl alcohol. Then a solution, isosmotic to a hypertonic solution, can cause some swelling of the cornea. Here we may assume a toxic influence.

In an experiment with a toxic substance known to affect the conditions of permeability strongly, digitonin, such an influence was evident. When 0.01-percent digitonin was added to a 1.4-percent solution of sodium chloride and the cornea bathed for 10 minutes with the solution no (or but an insignificant) decrease of the corneal thickness was found, as an average an increase of 3.1 percent. In comparison with the effect at the use of pure 1.4-percent solution of sodium chloride the difference in effect, 19.0 ± 4.1 percent, is significant.

It is a well-known fact that the cornea has a great swelling capacity. Isolated corneas will swell in aqueous solutions of sodium chloride and many other substances, even in blood serum and in solutions isotonic or hypertonic to this physiologic liquid as Cogan and Kinsey have shown (1942). The related experiments show that in the living eye, as these authors have shown on isolated eyes and corneas, solutions in contact with the corneal surfaces have a great influence on the state of turgescence of the cornea. It is evident that the surface layers must be of importance for the regulation of the turgescence.

Maurice and Giardini have studied that in important experiments where they have destroyed the limiting layers of the cornea in living rabbits. They found that when the epithelium was removed the thickness dropped about eight percent because of the thickness of the epithelium but after that there was a rapid increase with about 0.5 percent of the total thickness per minute

during the first hour. Then the rate of increase became markedly lower. The thickness reached a plateau at about 200 percent before the end of 24 hours and remained at this level for two to three days. Then there was a recovery phase lasting from one to four days when the thickness returned to the original level. It was seen that the epithelium regenerated and at last again covered the whole surface. One could observe that the cornea was thinner in those areas that were covered by epithelium than in the central denuded area.

If the endothelium was removed the increase in thickness was more rapid, in the beginning about 2.0 percent per minute and in three hours it was 100 percent, after which it soon reached levels above the method's capacity of measuring. In some cases the increase was still faster, about 3.0 percent per minute, and it was found that in these cases Descemet's membrane was also removed.

Thus measurements of the corneal thickness can be used for studying the water transport through the limiting membranes of the cornea. But in another type of experiment I have used it for studying the flow of water from the limbus (fig. 11). A sharp ring, nine mm. in diameter with a flange preventing it from cutting deeper than 0.4 mm., that is, the average thickness of a rabbit cornea has, by rotating movements, been forced into the corneal stroma of a narcotized rabbit and held in place by episcleral

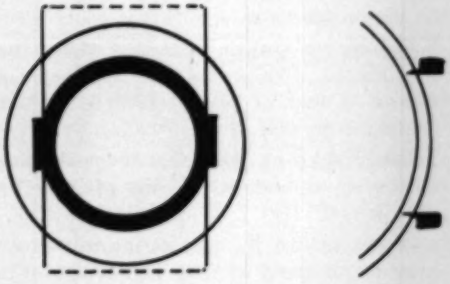

Fig. 11 (von Bahr). Measuring the flow of water from the limbus.

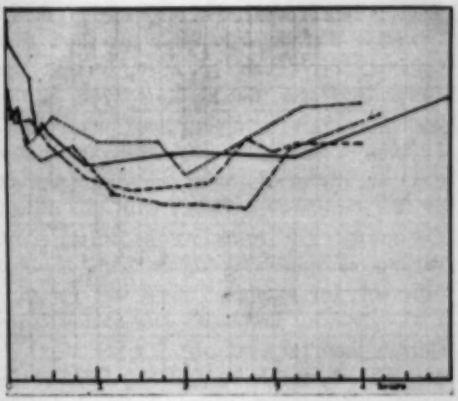

Fig. 12 (von Bahr). Graph showing results of the periodic measurement of the thickness of the central cornea.

sutures. When the thickness of the central cornea is measured periodically, it is seen that the thickness decreases until, after about three-fourths to one hour it reaches a plateau (fig. 12). About two hours afterward there seems to be a tendency to increase in thickness again.

What do these experiments show of the physiology of the cornea and how can their results be explained? Mainly they confirm opinions won in earlier investigations by methods which generally have been less physiologic. The experiment mentioned last shows that there is a decrease in thickness when a flow of fluid from the limbus is to some extent impaired by mechanical means. This means that fluid must leave the corneal substance through at least one of its surfaces and that fluid flows from the limbus toward the center of the cornea. That substances enter the cornea from the limbus is shown by others in many ways, the most physiologic one seems to be the modern one using radioactive ions such as Na^{24} which has been done by Potts and Johnson as well as Maurice. For this transport of water and other substances from the limbus into the cornea there is no reason to assume other forces acting than diffusion.

How the fluid leaves the corneal sub-

stances is less clear. There can be no doubt, however, that these experiments show that osmotic forces can be acting across the corneal surfaces, the limiting layers of the cornea acting as semipermeable membranes. If these membranes are destroyed either mechanically or by toxins the osmotic effect of the solutions in contact with the cornea disappears. The resistance to diffusion of various substances in these layers is very different, for example, much less for glucose, glycerin, and other fat-soluble substances than for electrolytes. (See also Cogan, Hirsch, and Kinsey, 1944.) Even if the layers act as if they were impermeable to many inorganic ions, for example, Na, it is now known that this is not quite true. The experiments with radioactive ions have shown that, for example, Na^{24} can pass these layers, but according to Maurice the resistance to diffusion can be calculated to be about 22,000 times greater than that of a layer of water of the same thickness. The resistance of the endothelium is 30 to 90 times less, still it is very considerable.

As water and other substances can diffuse freely from the limbus into the cornea, and the corneal stroma has a very great swelling capacity the still unsolved problem is: What keeps the cornea deturgescent? Cogan and Kinsey (fig. 13) have proposed the fascinating theory that the osmotic forces acting from the aqueous humor and the tear film are extracting water from the cornea through its surfaces. As the tear film could not act during night and measurements of the corneal thickness give the same value

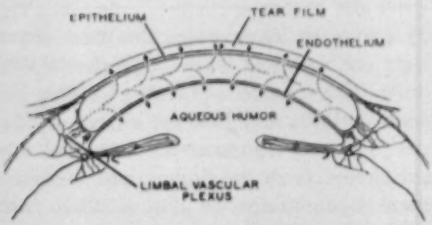

Fig. 13 (von Bahr). The movement of water into the cornea as suggested by Cogan and Kinsey.

just after the opening of the eye in the morning as in the middle of the day when it has been open for many hours, the aqueous humor must be important in this respect. I think that my experiments with bathing the anterior corneal surface with hyper- and hypotonic solutions, especially with regard to the results of bathing when the aqueous is replaced with air, support this theory. Evidently water can freely pass both the corneal surfaces in both directions. And evidently osmotic forces can act in both directions through the epithelium. If we compare the results of bathing corneas in contact with aqueous humor and those with air in the anterior chamber we find that water passes the posterior surface in both directions if there is aqueous in the chamber but not if there is air in it. If there were osmotic forces acting at the endothelium this would be quite natural. If we assume that there were some active transport, "secretion," at the posterior surface in normal eyes, we should expect it to work toward the air-filled chamber at least when the cornea by bathing with hypotonic solution is swelling, but it does not. This might speak against such an assumption. The fact that water enters the cornea from the aqueous humor when the cornea is bathed with a hypertonic solution shows either that the supposed active transport mechanism could act in both directions or that osmosis worked in this direction.

It is, of course, important to know if the aqueous humor is so hypertonic that it could be reasonable to assume that it could act to dehydrate the cornea. It is now stated that the osmotic pressure of the aqueous is in excess of that of plasma by a magnitude equivalent to that of three (Kinsey) to five (Duke-Elder) m M/L of sodium chloride. This gives an osmotic pressure of about 100 to 150 mm. Hg. The hydrostatic pressure working against it, that is, the intraocular pressure, is about 25 mm. Hg. It is said by Cogan and Kinsey that a mechanical pressure of about 30 mm. Hg will prevent cor-

neal substance from swelling in physiologic saline. It seems to me that the osmotic forces acting from the aqueous humor may be capable of holding the cornea deturgescent.

An objection to Cogan and Kinsey's theory that is often made (Davson, Maurice, Adler) is that if only water is extracted from the more central parts of the cornea they will be more rich in salts and then the osmotic pressure of the stroma is raised, so that water could no longer be attracted by the aqueous and tears. I do not believe that it must be so. If the tissue fluid is more concentrated toward the center, then the substances which have a higher concentration than that of the plasma will diffuse toward the limbus. A steady-state will be reached in which the concentration and consequently the osmotic pressure of the intracorneal fluid is between that of the plasma and that of the aqueous.

If this theory is right, the pathologic swellings of the cornea may be explained by damage to the semipermeable layers increasing their permeability. In some cases the cause may also be an increased osmotic pressure of the intracorneal fluid by an increased number of metabolites and other dissolved particles produced by inflammation. For the corneal edema in acute glaucoma with high tension an explanation may be that the osmotic forces attracting the corneal water cannot act sufficiently against the high hydrostatic pressure.

Before ending my lecture I should like to add a small practical hint given by the experiments:

In corneal edema it sounds reasonable to treat the patient by bathing his cornea with a hypertonic solution. It is proposed, for example, by H. K. Müller, that one should use a glucose solution. But according to my results it ought to be more effective to use a hypertonic solution of sodium chloride—I often use a two-percent solution—instead of glucose, for the corneal epithelium is less permeable to this salt solution than it is to glucose.

Discussion

Dr. Peter Kronfeld (Chicago): I have a very good opening quotation from the paper by Maurice and Giardini, the paper to which our distinguished speaker has referred several times (Brit. J. Ophth., **35**:169, 1951). This is the quotation: "Previous methods of measuring the corneal thickness in the living eye have recently been extensively reviewed and criticized by von Bahr, who devised an ingenious method of overcoming the practical difficulties and theoretical objections of its forerunners." Coming from a country known for its tendency toward understatements and coming from two persons who have worked in the field of corneal thickness for a number of years this statement is very significant.

The first few pages of Dr. von Bahr's paper are a lesson in physiologic optics that did me a lot of good. The paper then goes into the actual measurements and establishes an average thickness of the human cornea in vivo of 0.56 mm. The paper also establishes very clearly the fallacy of all measurements taken post mortem. What Dr. von Bahr's method measures is a very important characteristic of the cornea because corneal thickness is related to hydration and hydration is closely related to transparency. In other words, thickness is related to something that concerns us ophthalmologists very much.

The experimental work reported here by Dr. von Bahr is again a demonstration of osmotic effects upon the state of hydration of the cornea. His work differs from that of previous investigators in that it was done under more physiologic conditions and in a more quantitative manner. We are tempted to compare his work with that of George Smelser of New York who was interested in osmotic effects upon the cornea from the standpoint of contact lenses. He used eye baths with solutions of varying osmotic concentration. His criterion of the effect of those solutions upon the cornea was the development of haloes. With this method Smelser arrived at results and conclusions very similar to those of von Bahr. Distilled water produced haloes in a short time just as it produced marked thickening in Dr. von Bahr's experiments. His evidence, as presented here today, adds a great deal of weight to the Kinsey-Cogan theory.

Most of us have watched the Kinsey-Cogan theory develop, reach a peak of popularity, and gradually recede somewhat into the background because of the many objections raised. Still I was

happy to see that Francis Heed Adler in his last edition of the *Physiology of the Eye* had retained the Kinsey-Cogan theory. As an over-all concept I think it is of great value. To what extent the normal eye makes use of a strictly osmotic mechanism we still do not know, but the possibility of such a mechanism exists.

What perhaps should be brought out today is that there is not a great deal of divergence between the Kinsey-Cogan osmotic theory, on the one hand, and the so-called metabolic theory, on the other. Let us just think that through for a second.

For the osmotic gradient to be effective across the anterior surface of the cornea there has to be a certain degree of impermeability of the corneal surface. Cogan and Kinsey found such an impermeability with their methods which, admittedly, were not very physiologic. Permeability determinations made with other methods, primarily with tagged ions, by Maurice of England and by Potts and his associates of Cleveland have shown that the endothelium and the epithelium are fairly permeable to ions, particularly to sodium.

Now, does that really mean that there is no possibility of an osmotic gradient across the anterior surface of the cornea? Not necessarily. Dr. John Harris brought that out at the 1953 meeting of the Association for Research in Ophthalmology.

The situation in the cornea is similar to what takes place in and around an erythrocyte. For a long time we thought that the erythrocyte wall was highly permeable to anions and not permeable to kations, such as sodium. That concept seemed to explain adequately why the erythrocyte did not take up ions and water and burst. But then, by means of radioactive ions, a considerable passage of sodium into the red cell could be demonstrated. Thus it is not so much a question of permeability that maintains the characteristic kation milieu in the erythrocyte but a specific mechanism which is now called active transfer. In other words, diffusion of sodium probably takes place across the red-cell wall according to the rules of diffusion but on top of that there is a sodium pump that pushes sodium out of the erythrocyte. It is quite possible that a similar method of active ion transfer exists in the cornea. What used to be called impermeability is now called specific composition due to active ion transfer, but the over-all effect is much the same.

The difference between the two theories, the metabolic, on the one hand, and the osmotic, on the other, really is much smaller than it seemed to be four or five years ago. About that active transfer we had better not say very much at this point because in another year or so the Cleveland group, as well as Ussing at Columbia, may be expected to provide much more detailed information concerning ion transfer.

I would like to talk about a few possible applications of Dr. von Bahr's method. The problem that we want to tackle first is that of cornea guttata. Ever so often this condition is the only reason for the failure of an entirely uncomplicated operation. The cornea guttata was not recognized or not appreciated prior to the operation, but was made worse by the operative trauma so that the patient ends up with a full-blown epithelial dystrophy and no practical vision.

Cornea guttata in its milder forms is fairly common in the older age groups. It would be of great value to us if a method could be found whereby the severity of cornea guttata could be measured or gauged. It would seem quite possible to me that Dr. von Bahr's method of measuring corneal thickness may give us a way of gauging this disease. One might be able to prognosticate on the basis of measurements of the corneal thickness.

There is one other field in which I expect these measurements of the corneal thickness to be very helpful to us. Many of us have been asked to umpire contact-lens disputes. Both Dr. Smelser and Dr. McGraw had to face this problem. We are familiar with the fine work that was done by Dr. McGraw in the Army which was published in the *Transactions* of the American Academy recently. In situations of this kind an objective quantitative method is most helpful. The criterion used by Smelser is the development of haloes. You may remember, he designed an instrument for halometry. Another method which he used, in the study of the effect of contact lenses upon the cornea, was the determination of the turbidity of the cornea by measuring the diffuse light scatter. For that purpose, Dr. Smelser designed an instrument similar to the one now used by Langdon for fluorometry in the anterior chamber.

It would seem to me that the question of the most physiologic contact lens could be answered by measuring the thickness of the cornea. I think this measurement is very objective and should be just as sensitive as the development of haloes or diffuse corneal turbidity.

In the follow-up of corneal transplants I think measurements of the corneal thickness would also be valuable.

I myself am interested in the method for a reason which is more or less theoretic. During the last five years I have become engaged in tonometry under unusual conditions, that is, on the eyes of different species, corneas of different size and thickness. In this, actual measurements of the corneal thickness in vivo will be a great help to me.

It might be mentioned here that the method which was reported by Dr. von Bahr in 1948, is applicable to other measurements in the anterior portion of the human eye. A German author, Jaeger, adopted it to measurements of the depth of the anterior chamber. Again, by means of plane-parallel plates, he was able to focus simultaneously on the anterior surface of the cornea and the anterior surface of the lens. That method was pub-

lished in the report of the German Ophthalmological Society for 1951.

DR. A. E. MAUMENEE (Baltimore): I would like just to mention several other clinical situations in which this work is of great value.

In corneal transplants, when operating on patients with keratoconus, one of our main problems is to get the apposition of the wound edges between the donor and recipient tissue as close as possible. In the past we have tried to look at the cornea and to estimate where the apex of the cone was and then place the graft so that it would cover the apex of the cone. However, by the method described by Dr. von Bahr, and as it has been modified and simplified by Maurice and Giardini, one can actually measure the thickness of the cornea and decide how far or what size corneal graft has to be used to get outside of the very thin portion of the cornea and thereby get a better apposition. I think Dr. Phillips in England has been working on this particularly and has done some very good work.

I have also been interested in the point that Dr. Kronfeld mentioned in regard to patients with cornea guttata. I can tell you a practical part of what we have done and then probably offer some theoretic explanation for it, whether the explanation is correct or not I do not know. The practical part is that, in making a corneal section, that is in clear cornea and operating on a patient with cataract who has a cornea guttata, there is a much greater tendency for the cornea to become swollen and edematous following the cataract extraction. However, if in the same patient in the other eye with a similar cornea, a section is made well back in the sclera, actually entering the anterior chamber just over the base of the iris, or possibly just over the ciliary body, then there is much less tendency for that cornea to swell. I think that one possible explanation is that any human cornea, no matter how good the corneoscleral sutures are, tends to show damage at the posterior surface. You will see this by slitlamp and in a few histologic examinations of the eyes of patients who died during the second and third postoperative week.

The third type of patients in whom deturgescence of the cornea may be of value are those who have epiphora and epithelial edema over a long period of time. To cite a very good example: a young child when playing with a cap pistol, got some powder in the eye and there was a red mark of the pistol following this injury to the corneal epithelium. The hypertonic tears kept the cornea irritated and eventually the other eye became irritated and, after a period of three years, during which she had not been able to go out in the light, the cornea became superficially vascularized on both sides. After retrobulbar alcohol injection (95-percent alcohol) and deadening the pain fibers and the irritation of the cornea, it was possible to stop the epiphora and allow the tears to become hypertonic so that they did not cause swelling (as Dr. von Bahr mentioned with hypertonic solutions) and now, after a period of six months, her eyes have remained white and her vision has cleared to some degree.

DR. HARVEY THORPE (Pittsburgh) I, too, enjoyed Professor von Bahr's presentation, and I offer some simple questions and comments:

1. What was the variation of the corneal thickness at various distances from the apex toward the limbus; that is, what was the thickness of the cornea as measured by this method at a distance of three mm. from the apex and of five mm. from the apex, and so forth, as compared to the apical corneal thickness?

2. It was mentioned that this method can be used for determining the depth of the anterior chamber, and I wonder whether Professor von Bahr, who is most experienced with the method, has attempted to measure the depth of the anterior chamber and how applicable he found it.

3. I wonder whether the likely increase in the corneal thickness has been measured in the cases of Sattler's veil which are manifested by corneal epithelial and possibly stromal edema.

4. We see a good bit of endothelial dystrophy in this country. In some of these patients with early cornea guttata, or endothelial dystrophy, we find only morning epithelial edema of the cornea on biomicroscopy (aside from the posterior layer changes). The patient notices that vision is blurred on arising and that it clears as the day goes on. The intraocular pressure in these patients was found to be normal. In the past, some of these cases have gone on to rapid corneal degeneration after corneal surgery. Like Dr. Maumenee, I have used scleral sutures for some years. It has also been my observation that scleral incisions and sutures have reduced the incidence of corneal degenerations in cases of cornea guttata which come to cataract surgery. It would be interesting to know what the percentage incidence of this condition is in Dr. von Bahr's clinic.

I hope that Professor Goldmann can tell us where the simple apparatus (which he mentioned in discussion) can be obtained and also that Professor von Bahr will tell us where his apparatus can be obtained.

What is the increment percentage of experimental error of measurements made with the simple apparatus that Dr. Goldmann mentioned as compared to the one Dr. von Bahr uses?

DR. G. BIETTI (Parma): I would like to support the thesis my friend, Dr. von Bahr, has set forth in his very excellent paper. As you already know, one of my assistants, Giardini, has been working on the same topic for several years and there are some results which could not be quoted by Gunnar von Bahr because they were not yet published or they are just being published. One

special point was found regarding the influx of water into the cornea when you reduce the thickness of the cornea with diathermy or another injury at the limbus. From this experiment it was seen that the limbus circulation is of importance for the turgescence of the cornea. This was found only a few weeks ago.

Then there are also some other experiments which probably are not quite so important. We are also using this system of measuring the thickness of the cornea now for clinical purposes. And I think it is an important point because we have heard today very much about the physiologic aspect of the measurement of the cornea, but there are also many clinical facts. For instance, in regard to cataract surgery, there is always an increase in the thickness of the cornea after the operation but sometimes there is a large increase, sometimes a rather small increase. We were also able to draw a parallel between the presence of warts on the posterior surface of the cornea and the increase in the thickness of the cornea after cataract extraction. I do not know the explanation for this behavior. And when this increased thickness of the cornea after the operation is followed, one finds that sometimes it lasts for a few days or weeks and sometimes it lasts a much longer time without any specific reason.

DR. VON BAHR (Uppsala): I am not sure whether it would be possible to use these methods when there is a cornea guttata. I am afraid that the reflex image of the posterior surface would be very diffuse, very uneven, very irregular if the surface is not smooth and, in cornea guttata, it is of course very uneven. So there are still problems in measuring the cornea especially in cases with advanced pathologic findings.

When we can compare the images after wearing contact glasses, I think it will be possible to use this method. I have no experience in this field, as in our country contact glasses are rarely used and therefore I have not had an opportunity to study the problem. But I think we shall do it in the future. The same is true with corneal grafts as long as they are transparent. If they are not, it is impossible to measure these images, as we cannot get the reflex image from the posterior surface. If the corneal substance is a little opaque then we cannot see the reflex from the posterior surface. Thank you very much for your interest.

EPIDEMIC KERATOCONJUNCTIVITIS*

DESCRIPTION OF AN OUTBREAK IN AN INSTITUTION FOR THE AGED

JULIUS SCHNEIDER, M.D., ABRAHAM KORNZWEIG, M.D., AND MURRAY FELDSTEIN, M.D.
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Epidemic keratoconjunctivitis is one of the most contagious and disabling of the external ocular diseases. It was first described by Hobson in 1936. Since then, many local epidemics have occurred in shipyards, factories, and clinics, and have even originated in ophthalmologists' offices. The sporadic case is often atypical; many are probably misdiagnosed because of the absence of certain distinguishing features. Clinical appearances are most typical at the height of a local epidemic.

This is the first report of an outbreak in a home for the aged. We observed 16 typical cases of keratoconjunctivitis and four additional cases of follicular conjunctivitis toward the end of the epidemic which were not typical.

Kingsbridge House is a unit of the Home for the Aged and Infirm Hebrews of New York. There are three other units located in various parts of New York City. Several members of the medical, social service, and nursing staffs visit more than one unit in their daily routine. In spite of this, the epidemic remained completely limited to Kingsbridge House.

CLINICAL REPORT OF CASES

The ages of our patients ranged from 69 to 94 years. The sex ratio was two females to each male patient which is the same as the over-all ratio of inhabitants of the institution. In most instances there was first involvement of one eye followed in a few days by symptoms in the other eye. Two patients had the condition limited to one

* From the Medical Services of the Home for the Aged and Infirm Hebrews of New York. This work was supported by a grant from the United States Department of Health, Education, and Welfare. (B-154)

eye. The frequency of bilateral involvement was probably related to the transfer of the infection from one eye to the other by the patients as they wiped their eyes in spite of repeated warnings.

The first patient visited the eye clinic on November 19, 1953, for routine glaucoma follow-up. She had what appeared to be a follicular conjunctivitis of moderate severity in the left eye of one week's duration. Tension was taken using 0.5-percent tetracaine for local anesthesia. After the tension was taken, the tonometer plunger was wiped with 70-percent alcohol, the standard procedure at the home. Terramycin eyedrops and ointments were prescribed. The next day she had edema of the eyelids, redundancy of the mucosa, and serous discharge. Since with this treatment there was very little improvement, 0.5-percent Chloromycetin eyedrops were used, without benefit. The following week when the slitlamp examination showed multiple corneal infiltrates, the correct diagnosis was appreciated for the first time.

Nine days after her first visit, three other patients who had been in the clinic the same day as this patient showed early signs of a similar acute conjunctivitis. Between the 10th and 16th days there were four more cases, and during the 23rd to 41st days eight more patients were found to have an acute conjunctivitis. These latter patients acquired their infection after examination and treatment in the clinic and on the wards, but the time of infection could not be definitely determined. They had received tetracaine, pilocarpine, Chloromycetin, and terramycin eyedrops in the clinic prior to the development of their symptoms. One nurse, one attendant, and two other patients had a mild conjunctivitis without corneal involvement toward the end of this episode.

Clinical characteristics

The clinical picture was characterized initially by a sense of irritation in the eyes with redness and lacrimation. Objectively there was a varying degree of lid edema, chemosis, conjunctival redness, and redundancy with follicular hypertrophy. In three instances the discharge became serosanguineous. Adenopathy was not a prominent finding, the palpable preauricular glands appearing early, being rather small, and only slightly tender.

Two patients had pseudomembranes with subsequent complete clearing. One patient had true membrane formation. This eventually left residual scarring of the fornices. The conjunctival phase of the disease was from two to three weeks. Conjunctival scrapings of the first four patients showed mononuclear cells primarily of the lymphocytic type.

The corneal lesions often started as diffuse, superficial, punctate staining lesions. Later round subepithelial infiltrates were present both in the central and peripheral cornea. Most corneal lesions cleared in about four to eight weeks. In six patients, however, corneal lesions were still present after 12 months. The severity of the corneal lesion showed no relation to the degree of conjunctival disease. The final vision in all instances returned to the acuity which was present prior to the infection.

Treatment

Our patients were strictly isolated and treated with 0.5-percent terramycin or 0.5-percent Chloromycetin eye drops during the day and terramycin and Chloromycetin ointments were instilled at bedtime. These antibiotics appeared to have no effect on the course of the disease. Cold compresses were applied for congestion and edema. When corneal lesions appeared, 1.5-percent cortone ointment was given. Convalescent serum was not used. All eye drops throughout the home were discarded and no tonometer readings were taken for one month when the character of the outbreak was realized.

Discussion

This outbreak in a group of aged people was characterized by an acute onset, severe conjunctivitis, largely bilateral, and fairly

severe corneal involvement. Conjunctival recovery was slow as was corneal clearing. One third of the patients remained with corneal opacities after one year, but fortunately vision was not measurably affected by them.

It is impossible to determine whether the transmission initially was through contaminated eye drops or the tonometer. Subsequent cases were produced by eye drop infection. In all instances treatment did not alter the course of the disease.

In considering the incubation period, only the initial group of patients are being included because the time of contact for the latter group was uncertain. Our findings suggest that the incubation period was from nine to 16 days. Thygeson[1] found this to be seven to 10 days, whereas Feigenbaum[2] and also Sanders[4] reported it to be four to five days. On the other hand, Fried's[3] findings were three to 19 days, and Thorne's Bengal cases were 12 to 17 days. It is apparent, therefore that there is considerable variation in the incubation period.

The wide range of incubation period of three to 19 days reported by different observers suggests different etiologic agents in these epidemics. Sanders[4] isolated a virus in New York, Maumenee, et al.,[5] found their epidemic keratoconjunctivitis virus to be identical with herpes simplex virus. Ruchman[6] and Cheever[7] identified the causal factor with Saint Louis encephalitis virus. Following studies found no neutralizing antibodies to the Sanders or Ruchman viruses. Maumenee's findings likewise have not been confirmed.

Arakawa[8] in Japan isolated eight strains but Cockburn questioned his technique. Evidence thus far indicates that several viruses can cause epidemic keratoconjunctivitis under the proper circumstances.

It has been suggested that some sporadic cases and the initial atypical cases may be the reservoirs for subsequent epidemics. Then it is realized in retrospect that the early cases were atypical and the later ones more characteristic. Toward the end of our epidemic, cases became very atypical again.

Once started the rate of transmission is high. Cockburn, et al.,[9] reported a clinic epidemic among glaucoma patients with an attack rate of 23.5 percent when the tonometer was wiped with alcohol after tests. Pellitteri and Fried reported that 10 to 20 percent of contacts became clinical cases. Thygeson stated communicability is high due to the ability of the virus to survive drying and dilution.

There have been several reports of outbreaks of epidemic keratoconjunctivitis initiated and continued by the physicians and nurses treating groups of patients and transferring the viral agent through fingers, tonometers, and eye drops. In each instance, the reporting physician has used the standard soap and water hand wash, but there are no reported outbreaks when individual eyedroppers are used. This is the preferred method to avoid transferring infections in any office or clinic where large numbers of patients are seen. The technique of sterilization of tonometers is still unsatisfactory. We therefore continue to run the risk of having the ophthalmologists' offices and eye clinics serve as the source of spread of this very disabling condition. We now keep the tonometer in a Berens sterilizer with 1:5,000 benzalkonium chloride.

Summary

1. An outbreak of epidemic keratoconjunctivitis in a home for the aged has been described. It involved 16 cases in both men and women ranging from 69 to 94 years of age.

2. Special characteristics in this group were missing except that the keratoconjunctivitis was uniformly acute, severe, and very disabling.

3. Treatment is symptomatic and palliative. The antibiotics used seemed to have no specific effect on either course or duration.

4. Preventive measures found useful are:

a. Sterilization of tonometers by keeping

the tonometer plunger in a solution of 1:5,000 benzalkonium chloride or by heat sterilizing them in an alcohol-lamp flame.

b. The use of individual boiled eyedroppers for each patient.

c. Preventing suspected cases from touching arm rests, doorbells, equipment, and so forth in offices and clinics.

d. The surgical scrubbing of the hands with a bactericidal detergent (Phisohex) by all who handle a patient suspected of having epidemic keratoconjunctivitis.

11 East 68th Street (21).

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MASS TREATMENT OF TRACHOMA*

In Nara Prefecture, Japan, 1951-1954

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Introduction

Since historical facts have great influence upon trachoma in Nara district (Japan) some attention must be given to them.

According to ancient Japanese history, about 2,614 years ago, Yamato-Minzoku (the Japanese people) came to Japan from the southern district of Asia, and the Emperor Jinmu built the first capital of Japan at Unebi in the south-central part of Nara Prefecture where the Nara Medical College is located.

The Ainu race which had been living there before the Yamato-Minzoku settled in this district was deported to the north. Since then, a small number of Koreans and Chinese have migrated to this place, introducing their culture and Buddhism. Some of their descendants were later deported from the villages because they were leather-workers. In ancient times leather-workers were probably despised and abhorred by other people who believed in the doctrine of Buddhism. The deported leather-workers made a small village outside of the villages and lived in their poor shacks under unsanitary conditions.

In the 17th century, the Tokugawa government issued a proclamation that these outcasts were to be considered the lowest ones in the social order, that is to say, war-

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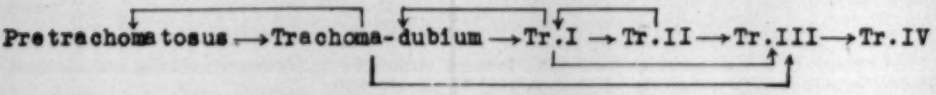
riors (Samurai), farmers, industrial workers, merchants, and the outcasts (called Etta), respectively.

The people belonging to this lowest rank were not allowed to have any land of their own for farming or to marry with others in higher ranks. In the Tokugawa era these outcasts were also the official executioners. For this reason, the general public of Japan showed great discrimination against them for many years.

After the Emperor Meiji ordered the cessation of this discrimination about 80 years ago, the outcasts were gradually able to get along well with the general public but they still cause a certain degree of social tension.

There now are 77 villages of these outcasts in Nara Prefecture (fig. 1) and the total number of persons is 53,034. This is about 6.8 percent of the total population of 763,883 in Nara Prefecture. This ratio is the highest one among all prefectures in Japan (fig. 2). In Nara Prefecture, the outcasts live in isolated villages which are crowded and dirty. Their houses (fig. 3) are poorly built so that their environment is quite unsanitary. Lack of proper sanita-



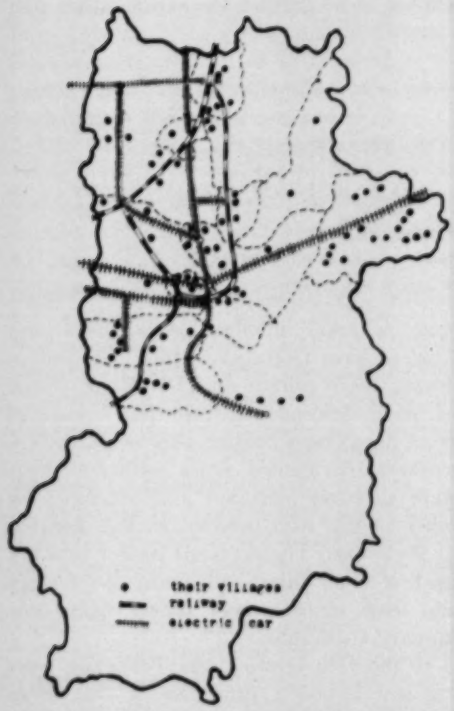


Fig. 1 (Kamiya). The location of the villages in Nara Prefecture.

Fig. 2 (Kamiya). Percentage of villagers in each prefecture in Japan. Number of villagers in unmarked prefectures is unknown.

Fig. 3 (Kamiya). Living conditions in the villages. (A) The houses had only a door, no windows, so that the inside was dark. (B) Cooking and dish washing might be done in front of the house. (C) Or the kitchen might be next to the wooden floor which served as a bed. (D) The latrine at the back of the house is in a state of ruin; it has no door.

tion is the chief cause of trachoma in this district. Most of the outcasts are shoemakers or day laborers.

In the big cities in Japan, the incidence of trachoma is so low that it is difficult to find a typical case of trachoma with serious inflammatory signs. However, according to official surveys, the majority of the outcasts, who live in the isolated villages, suffer from trachoma. Many reports submitted by ophthalmologists of the district indicate a frequency of trachoma among these villagers of close to 100 percent.*

Since ancient times in Nara Prefecture, these villagers have been called Akame which means red-eyes. This name is heard among us even now. It goes without saying that Akame (red-eyes) is the symptom of trachoma from which they are suffering. Most of these people believe that they are discriminated against by others only because of their red-eyes and also that, if they were free from trachoma, they would be treated fairly by others.

This is the reason why the governor of Nara Prefecture, Mr. Okuda, decided to institute a four-year plan to wipe out trachoma and to investigate scientifically the living conditions of the outcasts in order to plan further steps for improving them.

For this purpose, about eight thousand dollars were appropriated each year from 1951 to 1954 for mass trachoma treatment. During these years, 37 villages were chosen to test mass treatment of trachoma. Housing conditions were investigated while mass trachoma treatment was carried on. In addition,

* Hereafter in this paper the term "villagers" will refer to outcasts.

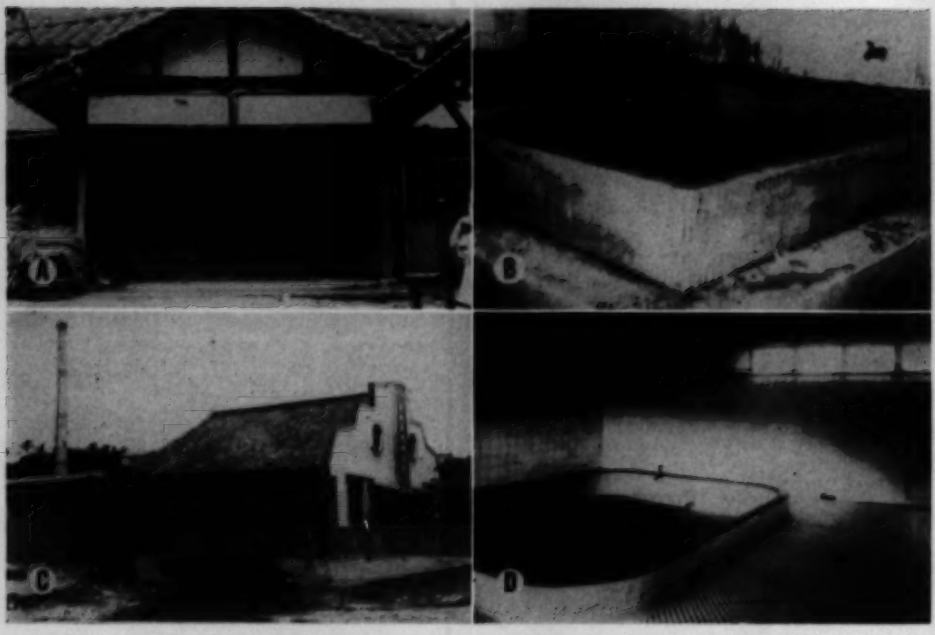


Fig. 4 (Kamiya). (A) Typical of the dilapidated bath house found in the villages, showing (B) the sort of tub in which about 900 villagers took a bath each day. (C and D) New facilities built for the villagers. The clean water for bathing comes from a newly dug well.

living conditions were gradually improved by, for example, construction of public bathhouses, roads, and ditches (fig. 4).

The results of this mass trachoma treatment were so remarkable that we received many thanks from the villagers and my assistants and I were honored on April 16, 1954, by the Educational Commission of Nara Prefecture.

Method of mass treatment of trachoma

Table 1 shows the 37 villages in which the mass treatment of trachoma was undertaken. A dispensary set up at the center of each village was open to all villagers from 5:00 to 8:30 P.M. over a period of one month. During this time all the pupils of the elementary schools were examined and treated. Each dispensary was operated by a mobile health team consisting of two ophthalmologists, two interns, and four nurses; in addition to this, one team was organized from the members of my department. Our team visited each dispensary, performing surgical operations for eye diseases. If we found diseases which required hospital treatment, such as cataract or glaucoma, we admitted the people to our hospital and treated them free of charge. (Most of the villagers are too poor to finance their treatments.) Every day at each dispensary, treatments were given directly by the doctors and interns to all the villagers who had chronic inflammatory conjunctival signs.

Crystalline aureomycin ointment (one percent, Lederle) was administered once a day under the lower lid in the majority of the patients, after the conjunctival sac had been washed out with one-percent NaCl solution. The remaining patients were given terramycin and chloramphenicol ointment in order to compare the efficiency of different drugs. Patients with long nails and dirty faces and hands were advised on personal

TABLE 1

DATA ON THE 37 VILLAGES IN WHICH MASS TREATMENT OF TRACHOMA WAS UNDERTAKEN

Name of Village	Duration of Treatment	Population of Villages	Total Number of "Fresh Cases"	Total Number of Times of Treatment§	Ratio of Patients to Population (percent)
Kanmaki, Mura	Nov. 28–Dec. 25, 1951	2,291	1,129	12,730	49.28
Iwamuko, Ouda-Cho	Mar. 24–Apr. 22, 1952	304	231	2,730	75.99
Kozuke, Ouda-Cho	July 21–Aug. 20, 1952	720	518	5,521	71.94
Tatsuichi, Mura	Aug 11–Sept. 10, 1952	1,060	664	8,849	62.64
Miyake, Mura	Aug. 22–Sept. 21, 1952	1,420	838	9,115	59.01
*Taima, Mura	Aug. 22–Sept. 21, 1952	†	678	10,375	
Okanishi-Mura	Sept. 12–Oct. 11, 1952	945	882	8,717	93.33
*Furuichiba-Cho, Nara-Shi	Feb. 2–Feb. 28, 1952	1,822	331	4,165	18.17
*Yokoi-Cho, Nara-Shi	Mar. 16–Apr. 18, 1952	688	302	4,335	43.90
*Katagiri-Mura; Yata-Mura	July 13–Aug. 12, 1953	2,784	1,390	12,830	49.93
Sango-Mura	July 13–Aug. 12, 1953	2,777	1,181	14,846	42.53
Ando-Mura	July 13–Aug. 12, 1953	1,575	990	13,512	62.86
*Gokyono, Tanbaichi-Cho	July 11–Aug. 10, 1953	951	533	7,680	56.05
*Isonokami, Tanbaichi-Cho	Aug. 11–Sept. 10, 1953	850	573	8,631	67.41
Heguri, Mura	Aug. 3–Sept. 2, 1953	929	470	5,339	50.59
Minamiikoma, Mura	Aug. 3–Sept. 2, 1953	401	348	3,023	86.78
*Funakura, Mura	Aug. 3–Sept. 2, 1953	805	724	10,775	89.94
Wakigami, Mura	Aug. 18–Sept. 16, 1953	1,749	1,048	12,162	59.92
*Hase-Cho	Nov. 20–Dec. 21, 1953	1,265	663	6,713	52.41
*Hachijo-Cho, Nara-Shi	May 7–June 10, 1953	525	328	5,904	62.48
*Nishinosaka-Cho, Nara-Shi	July 6–Aug. 10, 1953	780	455	6,210	58.33
*Umezono-Cho, Nara-Shi	Sept. 15–Oct. 21, 1953	328	219	3,800	66.77
*Higashinosaka-Cho, Nara-Shi	Nov. 6–Dec. 12, 1953	1,447	590	10,854	40.77
Shimonaga, Kawanishi-Mura	July 1–July 30, 1954	670	482	5,381	71.94
Umedo, Kawanishi-Mura	July 1–July 30, 1954	560	816	5,821	‡
Toyoda, Makimuku-Mura	July 1–July 30, 1954	538	414	4,037	76.95
Tenri-Shi	July 7–Aug. 5, 1954	498	361	4,356	72.49
Kanazawa, Kawahigashi-Mura	July 1–July 30, 1954	278	267	3,013	96.04
Daifuku-Mura, Kaguyama-Mura	Aug. 1–Aug. 30, 1954	1,965	851	6,967	43.31
Nishimatsumoto, Taisho-Mura	Aug. 1–Aug. 30, 1954	1,835	1,298	14,625	70.74
Kamada, Taisho-Mura	Aug. 1–Aug. 30, 1954	1,146	911	9,884	79.50
Kobayashi, Taisho-Mura	Aug. 1–Aug. 30, 1954	1,515	1,057	9,812	69.77
Iwasaki, Uda-Mura	Sept. 1–Sept. 30, 1954	1,549	715	4,849	46.16
Oshima, Gojo-Cho	Sept. 1–Sept. 30, 1954	1,200	607	6,084	50.58
*Katsuragi, Mura	Aug. 10–Sept. 10, 1954	449	212	1,993	47.22
Akebono & Daido, Yamato-Takada Shi	Nov. 16–Dec. 15, 1954	1,729	1,106	9,585	63.97
		40,348	24,182	275,673	

* Villages which were not completely isolated from ordinary villages so that some of them were included in or had contact with a big city.

† The record did not distinguish between outcasts and other people.

‡ Since other people came to the dispensary with these villagers, an exact ratio could not be made.

§ The patients were treated once a day so that the total number of daily patients is the same as the total number of treatments.

cleanliness. Several meetings were held with the villagers to discuss how to better their living conditions. Members of the Social Science Department and the prefectural authorities visited every nook and corner of the villages to learn conditions hitherto unknown because, until now, the villagers had not permitted entrance to their villages. When we became friendly with them, an anthropologist, Prof. Kohama, and his assistants measured some parts of the bodies of villagers without having them object.*

CLASSIFICATION OF CONJUNCTIVAL SIGNS

Even though the examinations were conducted with the aid of a hand slitlamp, the exact diagnosis of trachoma was very diffi-

* The results will be published independently by Prof. Kohama of Osaka University.

cult when the disease was in its initial stages. Therefore, without exactly diagnosing trachoma, all persons who had chronic inflammatory signs of the conjunctiva were treated. An individual record card was prepared for each patient with an evaluation of his clinical condition according to recommendations in my preliminary report (fig. 5). Various signs were graded by number as follows:

No. 1. No sign of conjunctival inflammation.

No. 2. A little roughness or redness near the outer and inner parts of the fornices, or some isolated follicles in the lower fornix.

No. 3. Slight roughness of the conjunctiva along the fornices, especially the upper fornix, with an occasional tiny follicle.

No. 4. Many tiny follicles buried in the conjunctiva and scattered over all the tarsal conjunctiva. This sign is identical with the condition referred to as the follicular type of Trachoma I (MacCallan).

No. 5. The slight roughness of the conjunctiva has spread over the conjunctiva from the fornix, with some inflammation, but scarcely any follicles can be found. This sign is identical with the condition referred to as the general lymphatic type of Trachoma I (MacCallan).

No. 6. Numerous grayish red excrescences protrude from all conjunctival surfaces. They are especially prominent at the upper conjunctival fornix.

No. 7. Papillary enlargements are seen over all the conjunctiva, predominantly with follicles, and beginning degeneration of the conjunctiva can be detected.

No. 8. The appearance of the conjunctiva is red, inflamed, and velvety. Individual excrescences cannot be distinguished, they are fused into a general infiltration.

No. 9. This is the stage of partial cicatrization which is probably identical with the condition referred to as stage III trachoma by MacCallan.

No. 10. This stage of partial cicatrization is identical to MacCallan's stage IV trachoma.

This classification is a modification of the basic classification proposed by MacCallan (fig. 5). All listed patients were re-examined once a week and on the final day of the month; the number describing the conjunctival signs was recorded each time.

1. Total number of patients observed

The total number of patients with beginning trachoma seen in one month at 37 dispensaries was 24,182, and the total number of daily patients in one month was 275,673. The ratios of patients to population of each village were from 40 to 96 percent, except in one instance which was 18.17 percent.

In order to evaluate the relative effectiveness of mass treatment of trachoma, some villages among the 37 were omitted from the detailed examination and calculation of the data. These villages* were not completely isolated from ordinary villages so that some of them were included in or had close contact with a big city; also, some of the villagers mixed with the ordinary people. The remaining 23 villages, in which there were no records that the inhabitants had received previous treatment, are the subjects of this study. The total number of patients in these villages during one month was 17,184, and the total number of daily patients in one month was 181,492; each patient, therefore, received treatments an average of 10.56 days in a month.

From the total number of newly infected patients, the total number of daily patients, and the integrate of the total daily patients in each dispensary (figs. 6, 7, and 8), it may be seen that the number of patients coming to each dispensary is similar. From this it was possible to estimate the total number of patients who received treatment in one month by checking the population of the villages and the number of patients seen on the first, second, and third days. It was then possible to estimate the total number of pa-

* Designated by an asterisk (*) in Table 1.

DIAGRAM OF THE STAGE OF TRACHOMA BY S. KAMIYA

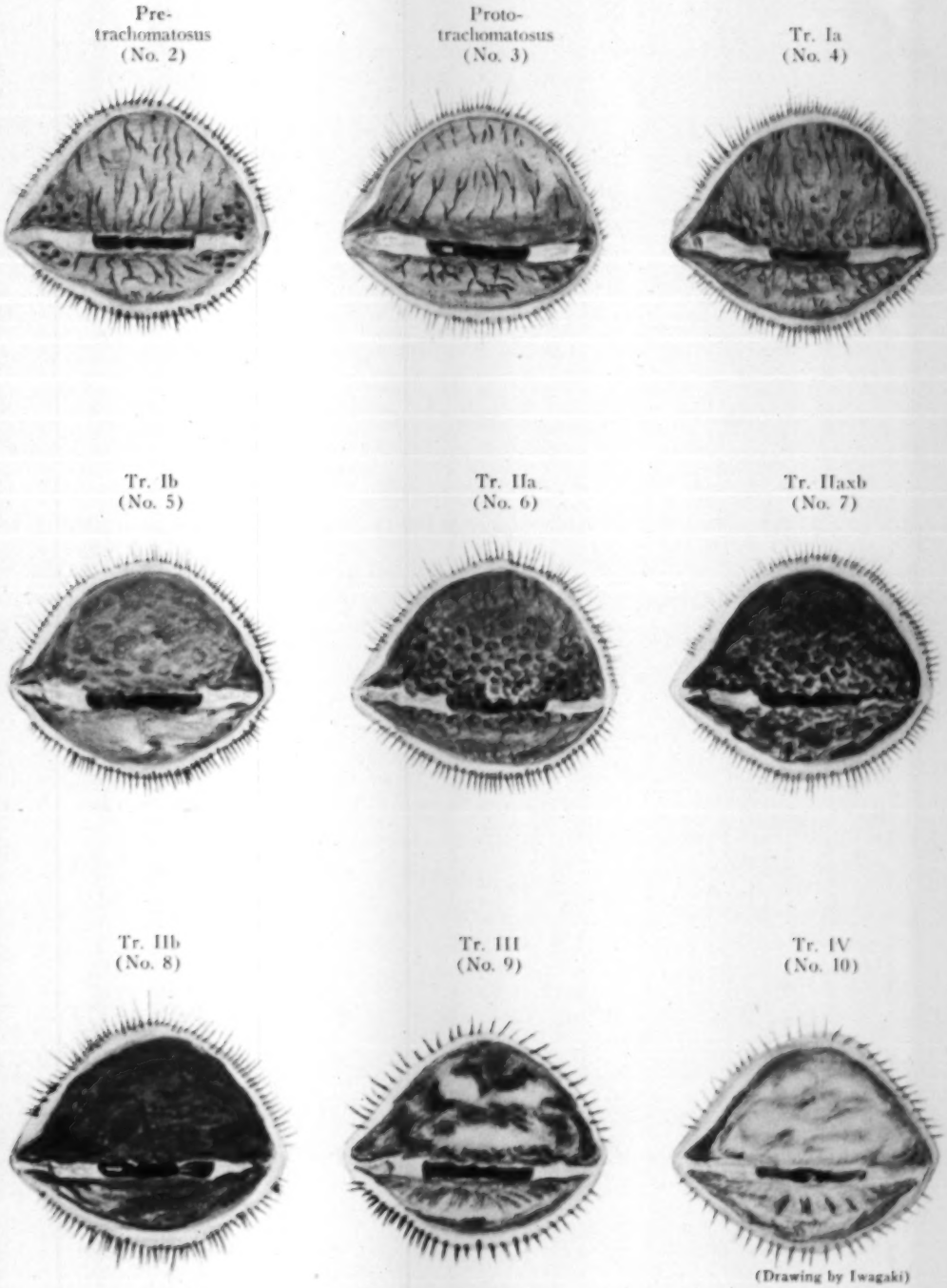


Fig. 5 (Kamiya). These drawings are from the preliminary report of this research published in the Acta of the Ophthalmological Society of Japan, **58**:1, 1954.

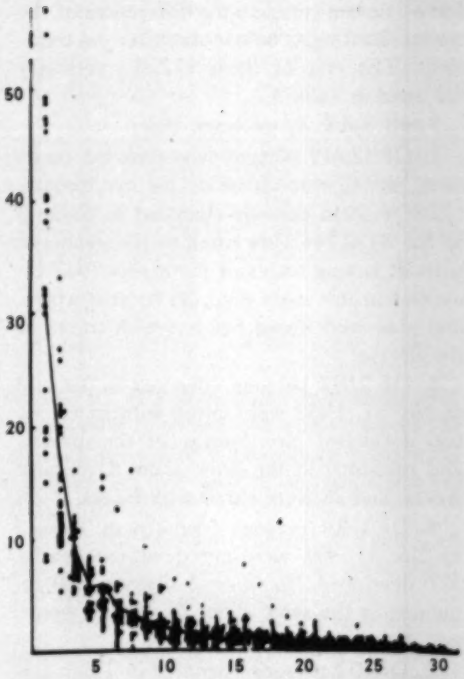


Fig. 6 (Kamiya). Diagram showing total number of patients with "fresh cases" in 24 villages.

tients who would come to the dispensaries, as well as the total number of treatments in a month, thereby making it possible to order

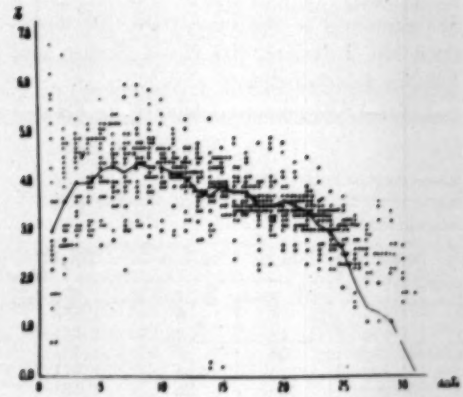


Fig. 7 (Kamiya). Diagram showing total number of daily patients in 24 villages.

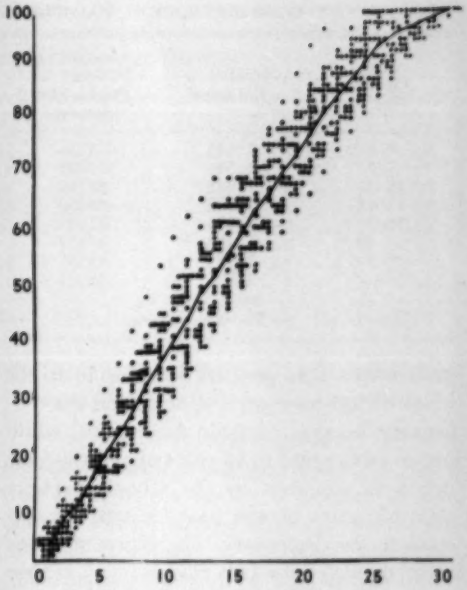


Fig. 8 (Kamiya). Diagram showing total daily patients at each dispensary.

an exact quantity of needed materials and drugs, effecting considerable economy.*

2. The relationship between age and clinical conjunctival signs

The full name and age of 15,082 patients were recorded and classified as shown in Table 2. From the second column, it may be seen that the number of the patients in each class is almost the same. Considering the ratio of patients to population in each age group, the young people, including students, are about 73 to 85 percent of the total population, however, youths and adults exempt from compulsory education are only about 27 to 33 percent. Persons more than 55 years of age are about 58 percent. This does not mean that more students suffer from eye disease than youths and adults. Rather, this

* The statistical method and results were published in detail in the *Journal of the Japanese Association against Trachoma*, January, 1956, pp. 1-6.

TABLE 2

AGE OF PATIENTS AND INCIDENCE OF TRACHOMA

Age Group (yr.)	Number of Patients	Ratio of Patients to Population (percent)
0–6	1,676	33.36
7–9	1,556	73.02
10–12	1,835	85.19
13–15	1,738	83.60
16–24	1,971	27.99
25–39	2,188	33.62
40–54	2,159	49.36
55–	1,959	58.01
Total	15,082	

ratio shows that persons between 16 to 49 years of age have no time to attend the dispensary because of their daily work, while pupils from seven to 15 years of age are compelled to attend it by the school; persons over 55 years of age have enough time to come to the dispensary. Therefore, all cases were divided into two classes: (1) Those who were forced to attend the dispensary, and (2) those who came of their own free will.

Table 3 shows the classification of the 15,082 cases into 10 catagories based upon inflammatory signs of the conjunctiva. It may be seen that the more seriously affected the older people were, the more frequently they attended the clinic.

3. COMPARISON OF THE CLINICAL SIGNS BEFORE AND AFTER TREATMENT

Among 15,082 persons, those who attended the dispensary only a few days are omitted, for we cannot compare the differences of the conjunctival signs before and after the treatment. The rest of them (12,319 persons) are listed in Table 4.

From Table 4, we learn that:

1. Of 12,319 persons who took the treatment, 4,590 were cured of the eye disease.

2. Of 3,716 persons (denoted in Table 3 as No. 2), 2,744 were cured by the treatment without having traces of the disease, 937 remained in the same state, 26 became worse, and nine were cured but left with traces of the disease.

3. Of 2,017 persons (denoted in Table 3 as No. 3), 1,058 were cured without traces, 636 developed No. 2 stage of the disease, 262 remained in the same state, 33 became worse, and 28 were cured with traces.

4. Of 1,401 persons (denoted in Table 3 as No. 4), 491 were cured without traces, 577 developed No. 2 or 3 disease, 270 remained in the same state, 22 became worse, and 41 were cured with traces.

5. Of 852 persons (denoted in Table 3 as No. 5), 196 were cured without traces, 340 developed No. 2, 3 or 4 disease, 195 remained in the same state, 26 became worse, and 95 were cured with traces.

6. Of 2,427 persons (denoted in Table 3 as No. 6, 7, or 8), 1,371 were cured with traces, only 91 were cured without traces, 583 remained in the same state, 105 developed No. 2 disease, 103 No. 3 disease, and 175 No. 4 or 5 disease.

7. Of 1,539 persons (denoted in Table 3

TABLE 3

CORRELATION BETWEEN AGE AND CONJUNCTIVAL SIGNS

Age Group (yr.)	Conjunctival Signs							
	No. 2	No. 3	No. 4	No. 5	No. 6, 7, 8	No. 9	No. 10	Total
0–6	802	378	269	121	102	2	2	1,676
7–9	700	320	283	125	122	6	0	1,556
10–12	791	436	292	132	170	12	2	1,835
13–15	733	402	261	137	170	28	7	1,738
16–24	694	447	251	159	302	114	4	1,971
25–39	484	330	210	134	491	483	56	2,188
40–54	193	150	83	76	641	878	138	2,159
55–	77	65	24	42	638	902	211	1,959
Total	4,474	2,528	1,673	926	2,636	2,425	420	15,082

TABLE 4

COMPARISON OF THE CONJUNCTIVAL SIGNS BEFORE AND AFTER TREATMENT

Conjunctival Signs before Treatment		Conjunctival Signs after Treatment									
		No. 1	No. 2	No. 3	No. 4	No. 5	No. 6	No. 7	No. 8	No. 9	No. 10
No. 2	3,716	2,744	937	22	3	1	0	0	0	6	3
No. 3	2,017	1,058	636	262	12	12	4	4	3	18	10
No. 4	1,401	491	387	190	270	13	2	5	2	27	14
No. 5	852	197	158	99	83	195	7	10	9	58	37
No. 6	742	73	61	68	62	26	151	24	17	163	97
No. 7	763	16	31	27	35	36	23	132	32	275	156
No. 8	922	2	13	8	4	13	2	21	181	439	239
No. 9	1,539	10	11	14	5	7	11	13	16	633	819
No. 10	367	0	2	0	0	1	0	3	2	17	342
Total	12,319	4,590	2,236	690	474	304	200	210	262	1,636	1,717

as No. 9), 819 were cured completely with traces, only 10 were cured without traces, 40 showed the severe inflammatory signs indicated by No. 6, 7, or 8, 37 showed slight inflammatory signs.

8. Of 367 persons (denoted in Table 3 as No. 10), 342 remained in the same state, and 25 showed inflammatory signs.

From these results it may be seen that the patients exhibiting conjunctival inflammatory signs show two effects of treatment: (1) Some were cured without traces of the disease; (2) some were cured with traces. The signs belonging to the first group are No. 2 or 3, those belonging to the second group are No. 6, 7, 8, or 9. Patients showing No. 4 or 5 disease demonstrated two tendencies: (1) Some of them were cured without having traces and (2) some of them were cured with traces.

So the tendencies of all conjunctival signs may be denoted by numbers and diagrammed as shown in Figure 9.

4. COMPARISON OF EFFECTS OF AUREOMYCIN, TERRAMYCIN, AND CHLORAMPHENICOL

As a result of adequate guidance for betterment of their living conditions, in addition to treatment, about 37 percent of the patients were improved after our one month of mass treatment, to the point where no inflammatory signs of the conjunctiva could be found.

These patients were observed closely once a week and their conjunctival signs were noted on their own cards. If these cards are arranged by the days which were needed to bring about no inflammatory signs, it may be assumed that the distribution of the days will obey a log-Gaussian distribution because the effects of the drugs on the biologic systems are usually proportional to the logarithm of the duration of the action of the drugs.

On the basis of this assumption, we made a plan to compare the effects of aureomycin,

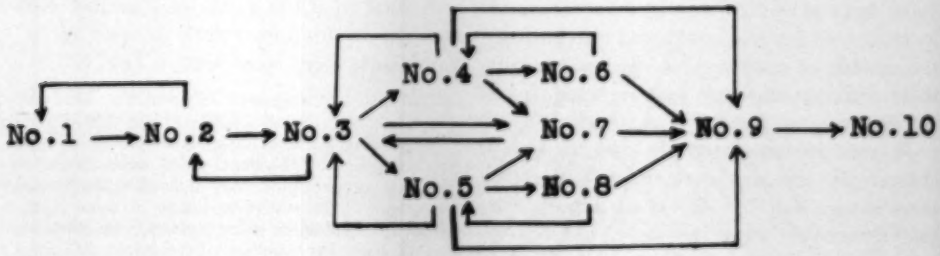


Fig. 9 (Kamiya). Diagram of the stages of trachoma. No. 1, cure without leaving traces. No. 2, pretrachomatosus. No. 3, trachoma dubium. Nos. 4 and 5, trachoma I. Nos. 6, 7, 8, trachoma II. No. 9, trachoma III. No. 10, trachoma IV.

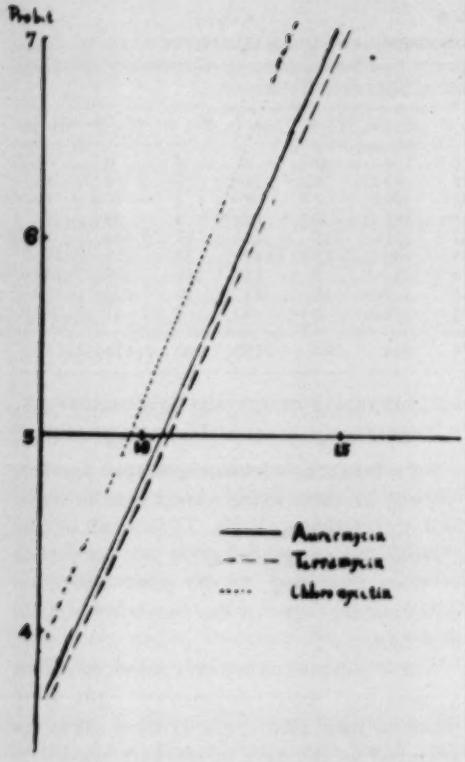


Fig. 10 (Kamiya). Diagram showing healing time in No. 2.

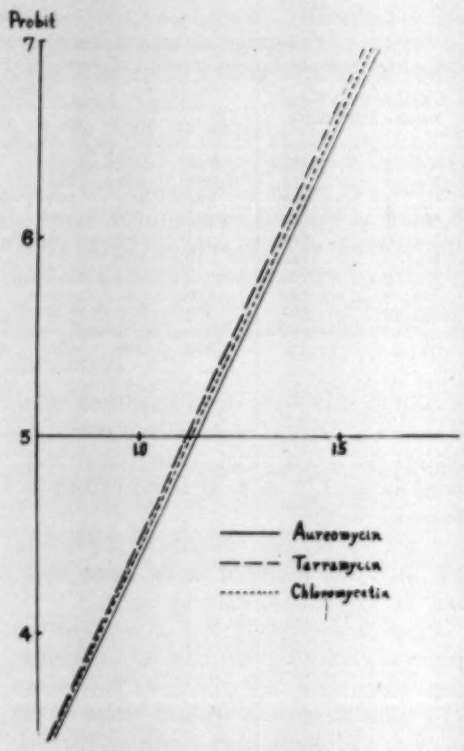


Fig. 11 (Kamiya). Diagram showing healing time in No. 3.

terramycin, and chloramphenicol by choosing three villages in which each drug was administered for one month. The results are listed in Tables 5A and 5B. The effects of each drug were compared by the Fisher-Bliss's probit analysis on the signs denoted by No. 2 and No. 3. Since the conjunctival signs denoted by Nos. 4 to 10 were not cured by treatment for one month and also because the number of cases was too small to confirm their distribution, they were omitted from the analysis.

It was shown that: On No. 2 signs, chloramphenicol was more effective than the other drugs, but the effects of aureomycin and terramycin were the same. On No. 3 disease, no difference in the three drugs was shown.

These findings seem to indicate that there are two components of the chronic inflammatory signs of the conjunctiva which have the same appearance—one is relatively sensitive to aureomycin and terramycin, the other less sensitive to them. In order to confirm this, the patients in the rest of the villages were treated with aureomycin only.

A total of 2,195 cases were treated with aureomycin for one month or until no inflammatory signs were present (fig. 12).*

* This diagram is obtained if it is assumed that the histogram of the days which were needed to treat the patients until they showed no inflammatory signs is the statistical image of some multimodal distribution, or more precisely, the combination of two log-Gaussian distributions of equal variances. This statistical treatment will be published in the *Journal of the Japanese Association against Trachoma.*

TABLE 5A

THE EFFECTS OF AUREOMYCIN, TERRAMYCIN AND CHLORAMPHENICOL ON THE CONJUNCTIVAL SIGNS DENOTED BY No. 2

Aureomycin

t	f	Σf	Σf/N	Probit
1– 7	99	99	22.65	4.2496
8–14	150	249	56.98	5.1759
15–21	112	361	82.61	5.9389
22–28	74	435	99.54	7.6045
29–	2	437	100.00	
	Regression line	y = 4.76147x + 0.00020	σ = 0.21002	
		m = 1.05014		

Chloramphenicol

t	f	Σf	Σf/N	Probit
1– 7	37	37	38.54	4.7089
8–14	31	68	70.83	5.5485
15–21	26	94	97.92	7.0739
22–28	2	96	100.00	
29–				
	Regression line	y = 5.14472x − 0.00021		
		m = 0.97191	σ = 0.19437	

Terramycin

t	f	Σf	Σf/N	Probit
1– 7	19	19	22.62	4.2486
8–14	32	51	60.71	5.2718
15–21	24	75	89.29	6.2421
22–28	9	84	100.00	
29–				
	Regression line	y = 4.67928x − 0.00047		
		m = 1.06864	σ = 0.21371	

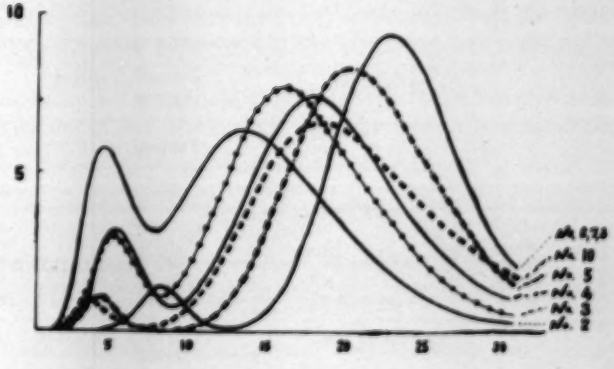


Fig. 12 (Kamiya). Diagram showing results in 2,195 cases treated with aureomycin for one month or until no inflammatory signs were present.

From the comparison of the six figures shown in Figure 12, we can see that the first component gradually becomes smaller, but the second component gradually increases as the number pertaining to the conjunctival signs becomes larger. The first components indicate 23.21 percent, 10.90 percent, and 11.63 percent in the conjunctival signs denoted by No. 2, No. 3, and No. 4, respectively.

According to our classification of conjunctival signs, No. 4 and No. 5 are referred to as trachoma I by MacCallan, No. 6, 7, and 8 are trachoma II, and No. 9 is trachoma III; No. 2 and No. 3 are not included in the definition of trachoma by MacCallan. We can also find the second component in the conjunctival signs denoted by No. 2 and No. 3.

In Japan, the conjunctival sign denoted by No. 2 (slight roughness or redness near the outer and inner part of the fornices; the remaining part of the conjunctiva showing no sign of inflammation) is diagnosed as "the stage I of trachoma," and this stage is found in 18 percent of our 12,319 cases. At this stage, the disease can be cured easily with penicillin and sulfathiazole or chloramphenicol. It has two components of which the second is likely to have some connection with trachoma; so it cannot be denied that No. 2 is trachoma.

If persons with trachoma (as shown by the second component of No. 2) are included, the frequency of trachoma in Japan will become very high and the frequency of healing trachoma by treatment will also become very high. To distinguish this second

TABLE 5B

THE EFFECTS OF AUREOMYCIN, TERRAMYCIN AND CHLORAMPHENICOL ON THE CONJUNCTIVAL SIGNS DENOTED BY NO. 3

Aureomycin

t	f	Σf	Σf/N	Probit
1– 7	26	26	9.29	3.6769
8–14	85	111	39.64	4.7373
15–21	97	208	74.29	5.6523
22–28	67	275	98.21	7.0992
29–	5	280	100.00	
	Regression line	$y = 4.38728x + 0.00068$ $m = 1.13983$	$\sigma = 0.22793$	

Chloramphenicol

t	f	Σf	Σf/N	Probit
1– 7	4	4	5.13	3.3665
8–14	24	28	35.90	4.6389
15–21	41	69	88.46	6.1983
22–28	8	77	98.72	7.2322
29–	1	78	100.00	
	Regression line	$y = 4.43807x + 0.00698$ $m = 1.12819$	$\sigma = 0.22532$	

Terramycin

t	f	Σf	Σf/N	Probit
1– 7	6	6	10.91	3.7687
8–14	16	22	40.00	4.7467
15–21	24	46	83.64	5.9802
22–28	8	54	98.18	7.0924
29–	1	55	100.00	
	Regression line	$y = 4.47167x + 0.00448$ $m = 1.11915$	$\sigma = 0.22363$	

component of No. 2 disease and to give it its true identity, I have termed it "pre-trachomatosus."

Comparing No. 2 and No. 3, we find that chloramphenicol acts upon No. 2 more effectively than aureomycin or terramycin, and that chloramphenicol could not be shown more effective in No. 3 disease. Under actual conditions it is rather difficult to diagnose No. 3 from No. 4 and No. 5. There are, however, many intermediate cases which we cannot diagnose as No. 2 or as having the typical conjunctival signs of trachoma No. 4 and No. 5 (referred to by MacCallan as the follicular type and the general lymphatic type, respectively). The sign denoted by No. 3 may be identified with proto-trachomatosus or trachoma-dubium, using the terms suggested by Wilson and Cuénod.

Most of the cases denoted by No. 2 or No. 3 have a tendency to be cured without leaving traces, as shown in Table 4. But No. 4 and No. 5 have two tendencies: Some were cured without leaving traces, usually changing into No. 2 and No. 3, and some of them were cured with traces, sometimes changing into No. 6, 7, or 8, with a strong conjunctival inflammation due to an unknown stimulus. It may therefore be said that the signs denoted by No. 4 and No. 5 are the beginning of the typical signs of trachoma.

By comparing incidence in age groups (table 3), we find that the conjunctival signs of No. 4 and No. 5 are high in the 10 to 15-year groups, which would seem to show that it takes several years for the typical appearance of trachoma to develop.

With respect to tendency to heal, there are some differences between No. 4 (follicular type) and No. 5 (general lymphatic type) the former heals more readily than the latter.

The inflammatory signs denoted by No. 6, 7, or 8 (stage II of trachoma by MacCallan) are more difficult to cure than the others (fig. 12). The highest frequency of trachoma II is in the 16 to 54-year age group so that it must have taken the disease 20 to 30 years to reach this stage. Most of the cases were cured with traces remaining but some of them improved to No. 4 or No. 5.

The trachoma stage III denoted by No. 9 was the most complicated one because, when it was cured with traces, the "traces" were still of serious nature and looked like an irregular "island," whereas, when the stage II (denoted by No. 6, 7, or 8) was cured with traces, the "traces" were merely many very fine lines.

Figure 13 diagrams the stages of trachoma.

Discussion

The frequency of trachoma among the ordinary people in Japan has decreased remarkably during the last 15 to 20 years, and, at present, the cases of typical trachoma amount to only a small percent among the pupils in the primary and secondary schools. However, when we entered the villages which we selected to test our mass treatment, we found that almost all the villagers had some chronic conjunctivitides. This fact is similar to the situation in Japan about 10 to 15 years ago when the ordinary people suffered from trachoma. We found many patients who had trichiasis, entropion, pannus on the cornea, and chronic dacryocystitis.

Our survey confirmed that the chief reason why the frequency of trachoma is higher among the villagers than the ordinary people is the difference in the living environment. This suggests that the cause of tra-

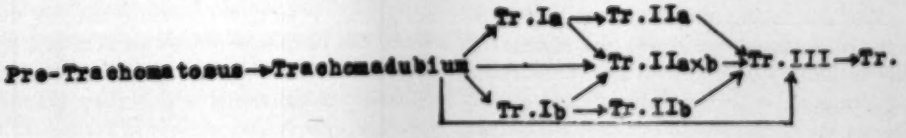


Fig. 13 (Kamiya). A diagram of the stages of trachoma. (a) General lymphatic type. (b) Follicular type. (a × b) Mixed type.

choma itself depends upon the difference in living conditions. This is confirmed by our survey in Nyudani, which showed that there is a clear difference in the signs of trachoma between the villagers who enjoy the same standard of living as the ordinary Japanese people and those who have a lower standard of living.

If we study Table 2 which shows the distribution of trachoma by age groups, we find that typical trachoma according to MacCallan's classification (No. 4 and No. 5 by our classification) can be seen in the older primary school pupils or in graduates from secondary and high schools.

Generally speaking, it seems to take many years for trachoma to develop into a stage with an entropion or trichiasis. And the conjunctival signs in the beginning stages (denoted by No. 2 and No. 3) are easily cured. If they develop into more serious cases, they are more difficult to cure.

Some authors claim that, if acute follicular conjunctivitis is caused by some agents (perhaps by a virus), it can be cured once without leaving traces of typical trachoma, or without developing into entropion or pannus; then, it shows the signs of conjunctivitis denoted by No. 2 and No. 3. However, if trachoma occurs again due to some other cause, it may be cured easily but it will develop into a chronic conjunctivitis by repeatedly undergoing cycles of remission and exacerbation; eventually, it will develop into typical trachoma.

The change from acute conjunctivitis to the chronic conjunctivitis will not be caused by a single event only, but by various stimuli, which may be viral elementary bodies or other material. If the stimulus is given repeatedly, the acute conjunctivitis will develop into the chronic conjunctivitis and then it will develop into typical trachoma.

Without taking this fact into consideration, we cannot explain why the villagers in the unsanitary district with a lower standard of living are more severely affected by trachoma than others with ordinary standards. For example, when the acute conjunctivitis was prevalent in pupils, both the ordinary children and the villagers' children were affected by it. But the children in the ordinary villages were completely cured without developing trachoma while the children in the villages developed trachoma. In our hospital, almost all the interns and nurses had been affected by acute conjunctivitis when they began to work at the mass treatment of trachoma, but they were never affected by trachoma.

Judging from these facts, we can say that the cause of trachoma is not only infection by a viral elementary body, but also the unnatural stimuli produced in an unsanitary environment. The human eye is so shaped that it is easily affected by dirty water, or smoke and dust. So, the ceaseless intrusion of these elements into the conjunctival sac will cause some slight inflammation to the conjunctiva.

What is the real counter-measure against trachoma? One important thing is to remove irritation to the eyes as much as possible by keeping the living environment clean, and another thing is to treat those who show inflammatory conjunctival signs as early as possible, however slight the signs may be.

During the mass treatment of trachoma in Nara Prefecture, the people were instructed on how to keep their living environment clean. The authorities assisted by building or improving the public bathhouses, by digging new wells and laying water pipes. As a result of these improvements, the frequency of trachoma among the pupils of the primary and secondary schools decreased from 60 percent to 10 to 12 percent at Kanmaki Village where the first treatments under the four-year plan of mass trachoma treatment were given. Our assumption was confirmed to be correct by this fact.

Now, let's consider the classification of trachoma. I wish to reiterate that in this study the conjunctival sign of No. 2 is not typical trachoma but the beginning stage of chronic conjunctivitis which may possibly develop into trachoma in the future. It is not claimed that it is not trachoma, but the

purpose is to distinguish it from trachoma; therefore, I named it "pretrachomatosus," the preliminary stage of trachoma. The conjunctival signs which could not clearly be distinguished from trachoma or pretrachomatosus would be diagnosed by us as "trachoma-dubium."

The present classification system gives the impression that trachoma is very easy to cure, studying only the results of the mass treatment reported herein, because it is very easy to cure the conjunctival sign No. 2. Using homosulfamin, as well as penicillin and other antibiotics (aureomycin and terramycin), it has been said that almost 70 to 80 percent of trachoma will be cured completely in a short time.

The difference in the classification of trachoma and the variations in the numerical data on the frequency of trachoma have resulted in disputes and confusion among the scholars of the Japanese Ophthalmological Association. Therefore, in order to compare our present-day data with the postwar studies by other Japanese scholars, conjunctival sign No. 2 must be included in the comparison. To compare this study with prewar data, conjunctival sign No. 2 must be excluded.

It is my opinion that pretrachomatosus and trachoma-dubium (No. 2) should be the object of the mass treatments and attempts should be made to eliminate it at its beginning stages because if No. 2 conjunctival signs are left unattended they will develop into trachoma, and if No. 2 signs are eliminated, trachoma will not occur.

Conclusion

By using aureomycin, mass treatment of trachoma was undertaken in 37 villages from 1950 to 1954. The treatment lasted for one month.

The result of the treatment of 24,182 patients shows that the occurrence of trachoma depends not only upon infection by a viral elementary body but also on unsanitary and dirty environments and repeated organic stimuli, or by the infection by various bacteria. Furthermore, there are no racial tendencies in trachoma.

At first, people are usually affected by conjunctivitis which is caused by dust, smoke, or dirty water entering into the conjunctival sacs. Though these signs may be cured easily, they indicate pretrachomatosus, which will occur at the slightest stimulus. If this state continues and is repeated many times, the uncurable and nonreversible signs of typical trachoma will gradually develop.

Typical trachoma with trichiasis or entropion will not occur suddenly. It could well take five to 15 years for the signs of typical trachoma to appear. At the stage which shows the reversible character, it can be cured without leaving traces but, when it becomes nonreversible, there will be more and more tendency to show cure with traces remaining.

The developing process of trachoma may be illustrated as follows:

Though the signs of pretrachomatosus are considered the first stage of trachoma in Japan, it is not typical trachoma, and it is better to treat it as an independent conjunctival symptom, distinguishing it from typical trachoma. It is quite natural to omit this sign from the record of the frequency of trachoma, but we had better treat this sign if we plan to prevent or exterminate trachoma.

Since unsanitary environments play important roles in the occurrence of trachoma, it goes without saying that we must treat not only the patients but their families and their villages as well.

In Nara Prefecture, we considered the villages the object of our treatment and improved the sanitary conditions. As we concentrated our efforts on educating the people in sanitation, in addition to treating them, we were able to get the remarkable results of our mass trachoma treatment.

I am grateful to the Governor of Nara Prefecture and his many officers for their kind co-operation in this work, I am also indebted in no small measure to the members of my own clinic for recording the data of this work. Finally, I owe much to my interns, students, and nurses for assisting me in this work.

CLINICAL PATHOLOGIC CONFERENCE*

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CASE HISTORY†

A 45-year-old white man requested removal of a cataract of the right eye.

PAST HISTORY

When the patient was first seen eight and one-half years prior to enucleation, he stated that since early childhood his right eye had turned inward and upward and a cataract had been present. No essential change took place in the condition of the eye until one year and four months before enucleation when he requested extraction of the cataract for cosmetic reasons and for possible improvement of his visual field.

PRESENT ILLNESS

Examination at this time revealed no vision in the nasal field probably as a result of macular changes. The left eye appeared normal in all respects. An intracapsular cataract extraction with a small iridectomy was performed. At operation the cataract was found to be of the hypermature type. The center of the anterior capsule was calcified and adherent to the temporal iris leaf. Delivery of the lens was difficult. Following delivery, a large gray fibrous tongue-shaped mass appeared in the posterior chamber from beneath the temporal area of the iris. This was excised leaving a clear black pupil. Postoperative funduscopic examination revealed a long black rope-shaped mass extending from the supranasal area to the macular region and a similar lesion extended from the supratemporal area to the macula. These lesions suggested old injury although no history of such an event could be elicited. The head of the optic nerve was atrophic. There were many vitreous opacities.

On the ninth postoperative day there was a small hemorrhage into the anterior chamber following a contusion to the eye. Some pain was noted in the eye on the 13th postoperative day. Examination six weeks after the operation revealed the same funduscopic lesions previously observed; the globe was clear and the eye was not painful. As before operation, there was only light perception.

Nine months after cataract extraction the globe became tender and inflamed, but within three weeks the inflammation subsided. The tension remained in the neighborhood of 18 mm. Hg (Schiøtz). About 11 months after cataract extraction a slight circumcorneal injection and a dome-shaped gray mass protruding from beneath the iris were observed. This lesion became more deeply pigmented and slightly larger during the next few months. There was no rise in intraocular pressure. Episodes of pain and redness continued. There appeared to be slight proptosis but no limitation of motion in any direction. No pulsation of the globe or edema of the lids or mucous membranes was noted.

LABORATORY EXAMINATION

Laboratory studies revealed no significant changes. Blood pressure was 160/78 mm. Hg.

COURSE

The right eye was enucleated one year and four months after cataract extraction. Following section of the four recti, the globe moved forward approximately one-half inch. Upon section of the optic nerve, the globe extruded itself from the orbit as if propelled from behind. Tenon's capsule appeared

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* From the Registry of Ophthalmic Pathology, Armed Forces Institute of Pathology, and the Episcopal Eye, Ear, and Throat Hospital. Presented during the postgraduate course in ophthalmology conducted by Col. John H. King, Jr., at the Walter Reed Army Hospital, February, 1955.

† From the Registry of Ophthalmic Pathology: AFIP Accession No. 615265.

much thicker than normal but the global surface was smooth and no orbital mass was found.

Differential diagnosis

Dr. Simpson

A man, aged 45 years, gave a history of his right eye having turned inward and upward and having been associated with a cataract since early childhood. Examination revealed an entirely normal left eye. Vision in the right eye was reduced to perception of light with faulty light projection in the nasal field. Removal of the cataract was requested for cosmetic reasons.

An intracapsular cataract extraction was performed with a small iridectomy. The lens was hypermature. Following delivery of the lens, a gray fibrous mass was removed leaving a clear black pupil. Examination of the fundus after operation revealed long black rope-shaped masses extending from the supranasal and supratemporal areas toward the macula. The optic nerve was atrophic. There were many vitreous opacities. Convalescence from the cataract extraction was interrupted by a small hemorrhage into the anterior chamber following a contusion.

Beginning nine months after the cataract extraction and continuing up to the time of the enucleation, there were episodes of pain and redness of the eye. There was never any rise in intraocular pressure. A gray mass which became slightly larger and somewhat pigmented was observed in the pupillary space.

The eye was enucleated 16 months following the cataract operation.

From this history the ocular problem might be summarized as follows:

The right eye was the site of a congenital situation such as hyperplasia of primary vitreous or of uveitis or endophthalmitis in childhood resulting in optic atrophy and cataract. Removal of the cataract was requested for cosmetic reasons. Cataract extraction was difficult not only because of adhesions at equator but also because of adhesions to the anterior surface of the vitreous.

The "large gray fibrous tongue-shaped mass" excised after the lens extraction was undoubtedly a cyclitic membrane or the membrane from a hyperplasia of the vitreous. The retina was detached and the optic nerve was atrophic.

The "dome-shaped gray mass which became deeply pigmented" during the next year was probably a cyst of the iris or, less likely, a downgrowth of epithelial tissue with a continuing detachment of the retina until it became complete. If this mass is retina, then cystic degeneration of the retina occurred. Mild attacks of recurrent uveitis, with some uncertainty as to the nature of the mass in the pupil, led to the enucleation. The intraocular pressure was never elevated throughout the postoperative period.

In my opinion, therefore, this patient had unilateral endophthalmitis in childhood which was severe enough to result in optic atrophy, secondary cataract, and a cyclitic membrane. The cyst of the iris or downgrowth of epithelial tissue was a result of cataract operation.

Diagnoses

Dr. Zimmerman

The 30 of you who turned in opinions included a great number of disorders in your differential diagnosis: traumatic implantation cyst (1), melanoma (5), other tumors (10), congenital malformations (3), traumatic lesions (3), specific infections (3), nonspecific inflammatory processes (3), and retinal detachment (2).

The *clinical diagnosis* was aphakia and large *iris cyst*.

Dr. Simpson's diagnosis is *cyst of iris* or *epithelial downgrowth* following extraction of cataract secondary to endophthalmitis in childhood.

My anatomic diagnosis is: *Epithelization of anterior chamber with cyst formation* following cataract extraction; long-standing flat detachment of retina probably secondary to injury in childhood.

Fig. 1 (Zimmerman and Simpson). The eye has been opened in the vertical plane and the temporal calotte removed. A cystic structure occupies the superior nasal portion of the anterior chamber. The atrophic iris is displaced posteriorly by the cyst. A gelatinous mass of degenerated vitreous is present behind the iris and the lens is absent. The vitreous is liquefied posteriorly. Gelatinous exudate fills the subretinal space. (AFIP Neg. No. 53-23778.)

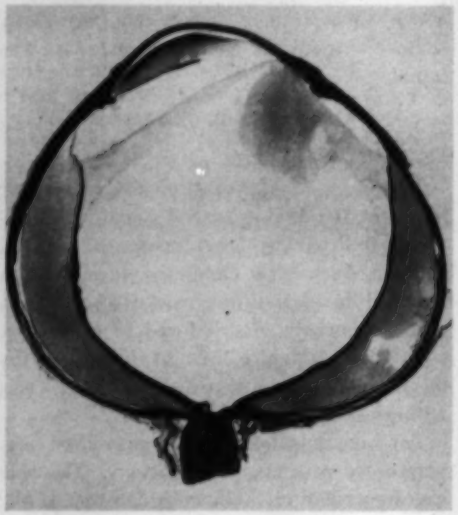

Fig. 2 (Zimmerman and Simpson). Celloidin section through central vertical plane of eye magnified two times normal size. A coloboma of the superior iris leaf is present but the plane of section does not include the cyst. (AFIP Neg. No. 55-4259.)

Pathology

Dr. Zimmerman

The lens and the "large gray fibrous tongue-shaped mass" that were removed unfortunately were not submitted for pathologic study. My report, therefore, is restricted to the anatomic changes observed in the enucleated eye. It was a large eye measuring 27 by 24 by 26 mm. Although the cornea was not clear, yellowish material could be seen in the anterior chamber. There was thickening of the superior limbus. The globe did not transilluminate. It was opened in the vertical plane.

The entire sensory retina was separated from the pigment epithelium by a glistening starchlike exudate which posteriorly was only one mm. thick but reached a thickness of three to four mm. along the equator (fig. 1). The sensory retina was a peculiar pale-buff color and appeared to be thickened.

Slightly elevated ridges extended from the posterior fundus to the periphery and these apparently were the explanation for the rope-shaped lesions described on fundu-

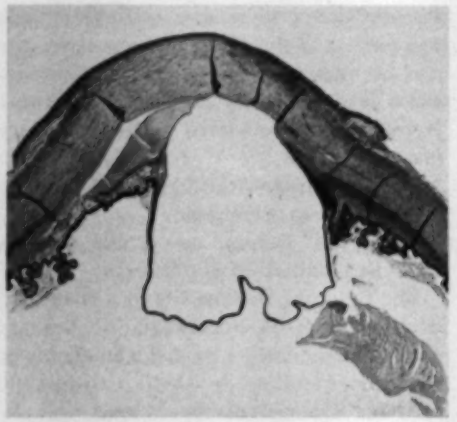

Fig. 3 (Zimmerman and Simpson). Paraffin section of nasal calotte showing thin-walled cyst of superior portion of anterior chamber. (X14. AFIP Neg. No. 55-4260.)

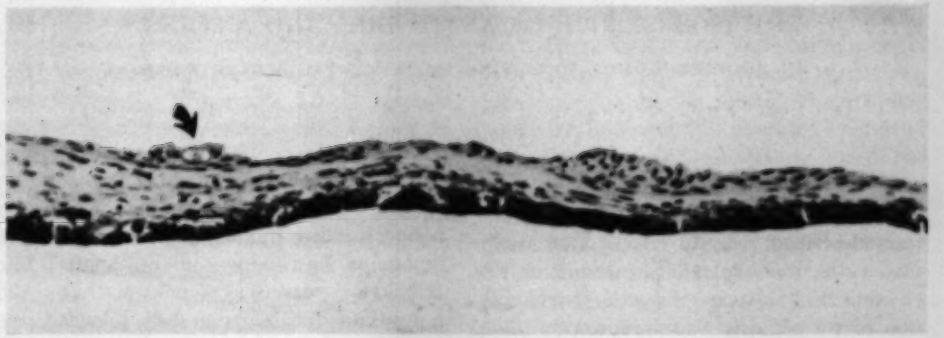

Fig. 4 (Zimmerman and Simpson). A segment of posterior cyst wall which is formed by an extension of conjunctival epithelium over the anterior surface of the atrophic iris. Arrow indicates a mucus-filled goblet cell. (×150. AFIP Neg. No. 55-4261.)

scopic examination. Most of the vitreous was liquefied. Anteriorly there was a mass of glistening opaque gray-white vitreous. No lens tissue was present.

Centrally there was a complete coloboma of the superior iris leaf (fig. 2). Adjacent to this was a large very thin-walled cyst within the anterior chamber (fig. 3). Its anterior wall was formed by the cornea while posteriorly it pushed the markedly atrophic iris far back away from its normal position. The cyst was lined by stratified squamous epithelium of conjunctival type. Occasional goblet cells could be identified in this epithelium (fig. 4). The retina showed evidence of long-standing detachment. Its color suggested siderosis, but iron stains were negative.

Discussion

Dr. Zimmerman

My conclusion in this puzzling case was that the patient (as suspected by his ophthalmologist) sustained an injury during childhood, probably a contusion. This caused partial retinal separation and a cataract. Following cataract extraction there was a downgrowth of epithelium from the conjunctiva into the anterior chamber where it formed a cyst.

Although this complication of cataract extraction has been recognized for a very long time and there are excellent clinical and pathologic descriptions in the recent literature,[1-3] it is still one condition that is seldom diagnosed before enucleation. We see this process regularly in our laboratory and about 200 cases have been collected in the Registry of Ophthalmic Pathology.

Dr. Arnall Patz has been conducting a clinicopathologic study of this material. He has very kindly provided some preliminary data concerning the first 130 cases studied. In only 29 of these was the epithelization suspected clinically. Glaucoma had developed in about two thirds of these eyes as a late complication; the retina was detached in one third. Dr. Patz has found some evidence of delayed wound closure as the most frequent complication in the immediate postoperative period.

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THE PERSISTENCE OF ANTIBODIES AND ANTIGEN*

IN AQUEOUS HUMOR FOLLOWING EXPERIMENTAL OCULAR TRAUMA

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INTRODUCTION

In rabbits specific ocular reactions have been described recently which were attributed to an immunologic phenomenon.[1] For eliciting these responses, a general sensitization of the animals was produced by injections of beef albumin, the eyes were traumatized, and then homologous antigen was given intravenously. This resulted in the development of a uveitis which could be produced only by the combined action of general sensitization and traumatization, but not by the action of either factor alone. In sensitized animals, antibodies were found only in the aqueous humor of the injured eyes but not in that of the normal eyes. From this it was concluded that the absence of detectable antibodies in the uninjured eyes is due to the inability of the antibodies to pass the intact blood-aqueous barriers.

The aim of the present investigation was to determine in the aqueous humor of rabbits, the length of time during which antibodies and antigens persist after ocular trauma.

METHODS AND MATERIALS

SENSITIZATION FOR ANTIBODY PRODUCTION AND TRAUMA PROCEDURES

The methods of sensitization and trauma application have been described previously.[1] Normal adult albino rabbits (two to three kg.) of either sex were injected intravenously and intramuscularly with bovine albumin (Armour) every third day for two weeks. One week after the last injection a nonperforating trauma was produced at the limbus of the right eye in each animal. The fellow eye served as a control. After the nonspecific inflammation had subsided, the animals were divided into groups of three. At different times each group was then skin-tested by intradermal injection of 0.1 ml. of 1:40 bovine albumin. Twenty-four hours after this procedure each group was examined once for specific antibodies in aqueous humor, iris, and serum. Aqueous humor, iris, and serum from the three animals of each group were pooled for each test. The tissues were homogenized (20,000 rpm for 10 minutes) in sterile saline so as to result in a 1:5 suspension by weight.

ANTIGEN DETERMINATION

The persistence of antigen (albumin) in the aqueous humor was determined in 10 test animals by injecting into each five ml. of 1:40 beef albumin intravenously. Immediately afterward, both eyes of each rabbit were subjected to a nonperforating trauma. The animals were divided into pairs. Aqueous humor was withdrawn from the first pair one hour later and from the other pairs after 24, 48, and 88 hours, respectively. The aqueous humor from both eyes of each rabbit was pooled and titrated using the agar diffusion technique described below. Controls consisted of aqueous humor from: (a) nontraumatized animals, which had received the same amount of antigen and (b) traumatized animals, which had not been injected with antigen.

AGAR DIFFUSION FOR ANTIGEN-ANTIBODY REACTIONS

The double diffusion method of Ouchterlony[2-4] was modified for this study. Bacto-

* From the Departments of Ophthalmology and Bacteriology, College of Medicine, The Ohio State University. This investigation was supported by a research grant, B-595 (c-1) from the National Institute of Neurological Diseases and Blindness of the National Institute of Health, Public Health Service.

agar was prepared as an 0.8-percent concentration with phosphate-buffered saline (pH 7.4) containing 1:10,000 merthiolate. After autoclaving for 10 minutes, 5.0 ml. aliquots of the agar were poured and solidified in petri dishes.

Filter paper assay discs were saturated with three to four drops of either aqueous humor or iris suspension or serum and then dried under vacuum. This procedure was repeated. Subsequently, the discs were placed in the center of an agar plate and additional humor, iris suspension, or serum was applied onto the discs. Other discs were placed radially at 7.0-mm. distances from the central disc and saturated with dilutions of the test antigen (bovine albumin 30 percent). It was necessary to use dilutions of the antigen since precipitates form in the agar only when the reactants are present in equivalent proportions. An excess of one of the reactants (usually antigen) prevents precipitation. Also, the reaction may occur under the serum saturated filter paper and thus escape observation.

The plates were covered with lids and incubated at refrigerator temperature. Observations were made daily for 14 days by viewing the plates in oblique light. Sudden changes in temperature were avoided since artifacts may result. Lines of precipitate were observed between the antigen and antibody discs as early as the second day. Often the precipitates seen with the aqueous humor faded after six to seven days due to continued diffusion of antigen effecting a zone of antigen excess. In some tests, the sera were not concentrated since their antibody content was adequate.

The same method was used to determine the presence of *antigen* in aqueous humor. In this case, the aqueous humor was used as the antigen source whereas rabbit antibeef albumin served as the source of antibody.

Results

After ocular trauma, *antibodies* in the aqueous humor persisted for seven days (table 1). The same antibodies could be demonstrated in the serum for at least 28 days. There was a close correlation between skin sensitivity and the presence of circulating antibodies in the serum. Marked skin reactivity, however, still persisted even after immune substances from aqueous humor had disappeared. When serum antibodies were no longer apparent, skin reactivity diminished until it approximated that found in nonsensitized rabbits. Neither fixed nor circulating antibodies could be detected in the iris homogenates.

After ocular trauma, *antigen* could be detected in the aqueous humor for the first 18 hours but not beyond this period (table 2). The nontraumatized control animals which were injected with albumin showed no antigen in the aqueous humor (table 2, 880, 874). Moreover, no antigen was found in the aqueous humor of the control animal which received an eye injury but no intravenous albumin (table 2, 869).

Discussion

It has been demonstrated in these experiments that antibodies and antigen may remain in aqueous humor for a significant period after an experimental injury to the eye. The antibodies and antigen found in the aqueous humor apparently transude from the blood serum when the blood-aqueous barrier breaks down as a result of ocular trauma. This may explain why clinical uveitis could be complicated by subsequent exposures of the sensitized eye to homologous antigen.

The length of time during which antigenic substances persist in the aqueous humor appears sufficient to permit a fixation of antibodies to ocular tissues. This could lead to an antigen-antibody combination with a resultant local tissue damage. It is well known that, with presently available techniques, it is very difficult to demonstrate the presence of fixed antibodies in tissues. These difficulties may account for our failure to find antibodies fixed in the irises of sensitized animals.

The mechanisms available in the eye for

TABLE 1

PRESENCE OF ANTIBODIES DETERMINED WITH THE AGAR DIFFUSION METHOD

	Antibody Source		Antigen for Agar Diffusion Bovine Albumin (30%)‡	Average Skin Reactivity at 24 hr.
	Aqueous (concentrated)			
30*/7	Pool 1 (three rabbits)	OS	−	42 by 35 mm. with necrosis
		OD†	+	
	Pool 2 (three rabbits)	OS	−	37 by 37 mm. with necrosis
		OD	+	
	Pool 3 (three rabbits)	OS	−	25 by 25 mm. with necrosis
		OD	+	
	Serum (not concentrated)			
	Pool 1		+	
	Pool 2		+	
	Pool 3		+	
	Iris			
	Pool 1	OS	−	
		OD	−	
	Pool 2	OS	−	
		OD	−	
	Pool 3	OS	−	
		OD	−	
51/28	*Aqueous* (concentrated)			
	Pool 4 (three rabbits)	OS	−	47 by 45 mm. with necrosis
		OD	−	
	Pool 5 (three rabbits)	OS	−	33 by 33 mm. with necrosis
		OD	−	
	Pool 6 (three rabbits)	OS	−	40 by 40 mm. with necrosis
		OD	−	
	Serum (not concentrated)			
	Pool 4		+	
	Pool 5		+	
	Pool 6		+	
	Iris			
	Pool 4	OS	−	
		OD	−	
	Pool 5	OS	−	
		OD	−	
	Pool 6	OS	−	
		OD	−	
72/50	*Aqueous* (concentrated)			
	Pool 7 (2 rabbits)	OS	−	7 by 6 mm.
		OD	−	
	Pool 8 (4 rabbits)	OS	−	3 by 2 mm.
		OD	−	
	Serum (concentrated)			
	Pool 7		−	
	Pool 8		−	
	Controls (2 normal rabbits)			2 by 3 mm.

* Ratio of: Number of days after which antibodies were determined following initial sensitizing dose / Number of days after which antibodies were determined following ocular trauma.

† OD indicates eyes which were traumatized.

‡ Plus (+) indicates presence of antibodies.

TABLE 2

PERSISTENCE OF INTRAVENOUSLY INJECTED ANTIGEN IN AQUEOUS HUMOR FOLLOWING OCULAR TRAUMA

Rabbit Number	Hours after Trauma Sample Obtained	Reaction with Agar Diffusion Technique*
879	1	+
881	1	+
880 (Control—no trauma)	1	–
856	18	+
872	18	+
874 (Control—no trauma)	18	–
875	24	–
857	24	–
869 (Control—no albumin)	24	–
858	48	–
865	48	–
868	88	–
859	88	–

* Plus indicates presence of antigen.

the removal of foreign antigenic substances may explain the relatively limited period (18 hours) during which antigen could be found in the aqueous humor after ocular injury. First, antigen, being suspended in the ocular fluid, would drain with the aqueous humor through the angle of the anterior chamber. Second, the antigens would probably be removed by macrophages of the uveal tract.

The antibodies tested in the experiments reported here were of the precipitin type. This was verified by making parallel tests with sera from the sensitized animals against homologous antigen by the conventional ring method and the agar diffusion method of Ouchterlony.[2-4]

The advantages of the agar diffusion technique for the present study should be pointed out:

1. It permitted the use of very small quantities of aqueous humor and antigen.

2. Despite the small amount used in this test, its sensitivity equalled that of the classical precipitin ring test.

3. Since aqueous humor contains only very small amounts of proteins, this method allowed concentration of gamma globulin which might be present.

SUMMARY

Rabbits were sensitized with beef albumin and their eyes were traumatized. Upon subsequent intravenous injection of beef albumin, antibodies appeared in the aqueous humor and persisted for seven days. Intravenous injection of antigen (beef albumin) was detectable in the aqueous humor of nonsensitized rabbits for 18 hours after ocular trauma. The presence of antibodies and antigen was demonstrated by the agar diffusion method of Ouchterlony which was modified for the testing of these substances in aqueous humor.

Department of Ophthalmology (10).

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OPHTHALMIC MINIATURE

A little debt will make you industrious and furnish you with an excuse to send in your bills as soon as your patients recover.

Benj. Rush, Letter to D. Petrikin, 1812.

SWELLING AND DISSOLUTION OF THE RABBIT CORNEA IN ALKALI*

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In the course of a study of the effects of alkali burns upon the cornea of surviving experimental animals, it became desirable to compare the effects of topical in vivo application of alkali with the more drastic procedure of prolonged and complete immersion in vitro of the excised cornea in alkali. With respect to the in vivo experiments, this paper limits itself to short term effects, directly after burning (Section 8).

1. TECHNIQUE

Adult rabbits of both sexes, and diverse coat colors, were killed by the injection of air into a marginal ear vein, and corneal buttons were dissected out at the limbus. Fourteen animals were used. The cornea was weighed on a torsion balance, nominal range 0 to 500 mg., sensitivity 0.1 mg. The range could be extended to 1.0 gm. by the use of a supplementary counterweight. The cornea was immersed in the alkali solution in a syracuse watch glass, and at intervals thereafter was taken out, blotted carefully with filter paper to remove excess moisture, and weighed. The weighing usually could be done in less than one-fourth minute. The weight of the freshly excised cornea varied from 42.2 to 62.4 mg., averaging 52.9 mg.

2. EFFECT OF M/1 ALKALI

The concentrations of alkali used were M/1 and M/5 NaOH. A 0.9-percent NaCl solution, approximately isotonic with mammalian blood, is 0.154 molar. Hence M/1 and M/5 NaOH are both hypertonic, and if any observed effects were to be expected on the basis of osmotic pressure alone, one would expect a shrinkage of the corneal buttons. Only swelling occurred.

The cornea clouds immediately on immersion into alkali, but remains partly translucent. As shown in Figure 1, after immersion into M/1 NaOH, a rapid and considerable swelling occurs, which appears to commence immediately upon contact with the solution. The experiments illustrated were carried out at room temperatures, which varied from approximately 28.5 to 31.7°C. The open and closed circles represent corneas of O.D. and O.S. of the same animal. Swelling progressed at a regularly declining rate for approximately four hours, and was followed by a much more rapid dissolution phase which was completed in less than an hour. In going into solution, the cornea changed from a relatively firm gelatinous consistency to a very soft mass. At maximal swelling, the corneal weights were of the order of 200 mg.

3. INITIAL SWELLING RATE

For the interpretation of histologic ob-

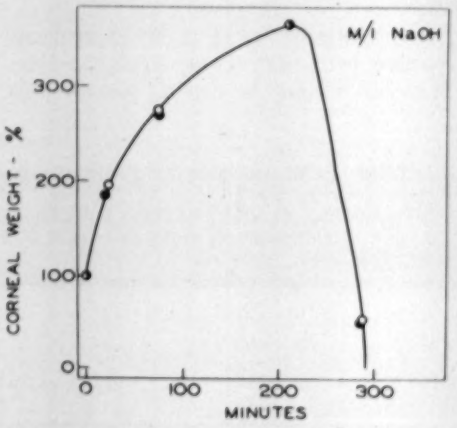

Fig. 1 (Shapiro). Swelling and solution of rabbit cornea in M/1 NaOH. Temperature 28.5 to 31.4°C. Open circles, left cornea. Closed circles, right cornea. The dissolution phase is indicated by the descending limb of the curve.

* From the Department of Research, Wills Eye Hospital. Aided by a grant from Vida Lodge, Philadelphia, Pennsylvania.

servations, it is of interest to calculate the initial swelling rate, that is, the period comparable to the early stage of an alkali burn, when the alkali has not yet begun to be washed out of the eye. A tangent ruled at the beginning of the curve showed an initial swelling rate dw/dt (w = weight, t = time) of 5.5 percent per minute. This is the period when first-aid attempts to save the eye from the consequence of alkali burns are usually most actively taken. At the end of the first hour, the swelling rate has declined to 1.1 percent per minute, whereas at the second and third hours the rates are respectively 0.76 percent and 0.55 percent per minute.

4. Histologic picture

One cornea was fixed in Bouin's fluid at the time of maximal swelling, in M/5 NaOH, 420 minutes after immersion, when its thickness was approximately 3.5 mm., and it had swollen to 413 percent of its original wet weight. The tissue was prepared by the paraffin technique and a section parallel to the surface is shown in Figure 2. The lower power view (×44), Figure 2A, reveals the vacuolization occurring in the substantia propria. Numerous small patches of varying sizes, which stain more deeply, are visible in the central area of the cornea. The area outlined by the dashed-line rectangle is contained in Figure 2B (×125) and shows the large variation in the size of vacuoles developed. The large weight increase exhibited by the corneal buttons during alkali immersion is consequently due in part at least to the accumulation of aqueous fluid within these vacuoles of the corneal stroma. Another element of weight increase probably arises from imbibition of the stromal protein (see Discussion for a consideration of protein swelling).

In contrast with the above, a cornea was fixed in Bouin's fluid, after only five minutes in M/1 NaOH, and prepared by the paraffin technique. Examination of such sections reveals an incipient vascuolization process under the corneal surface, but no appreciable vacuolization, in the stroma, comparable to that of Figure 2. These sections serve as a form of control to demonstrate that the vacuoles appearing in Figure 2 were not induced by prolonged exposure to the constituents of the fixative (picric acid, acetic acid, formaldehyde).

5. Effect of alkali concentration

In weaker alkali, of one-fifth the concentration, a similarly rapid swelling occurs, the tissue requiring roughly twice as much time to attain its maximum weight. Instead of dissolving shortly thereafter, the plateau is maintained for about 20 hours, and solu-

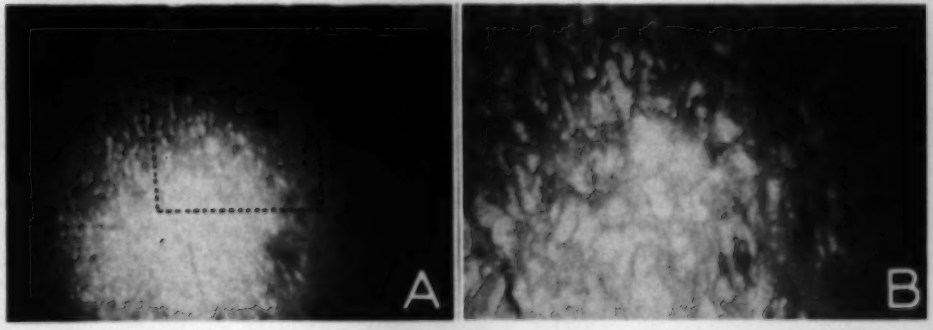

Fig. 2 (Shapiro). Microscopic appearance of rabbit cornea after swelling 420 minutes in M/5 NaOH, to maximal size. (2A) ×44. (2B) ×125. The area enclosed within the rectangle in (A) is shown enlarged in (B).

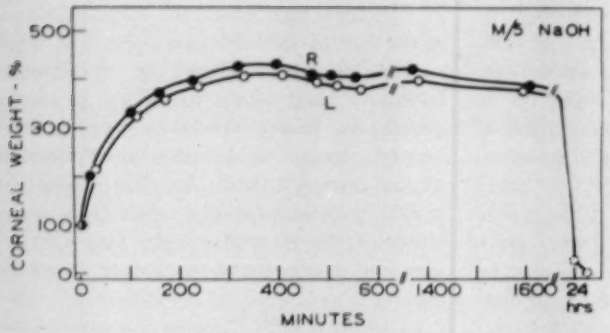

Fig. 3 (Shapiro). Swelling and solution of rabbit cornea in M/5 NaOH. Temperature 31 to 34.5°C. Open circles, left cornea. Closed circles, right cornea.

tion of the tissue subsequently sets in, as is evident in Figure 3. At the end of one day most of the cornea has dissolved, and the process is practically complete during the following day. The initial swelling rate, 4.8 percent, is approximately the same as for the M/1 swelling.

6. Influence of temperature

By placing the corneas in the cold, the course of dissolution of the corneal tissue is very significantly retarded. In six rabbits, the cornea of O.S. was left at room temperature (29.6°C.) immersed in M/1 NaOH, and it behaved as previously described, undergoing complete solution in a period of hours. Had they been left at body temperature, 37°C., the solution of the cornea in the alkali would have been still more rapid. The O.D. corneas were likewise immersed in M/1 NaOH, and placed in a refrigerator at 11°C. Examined 19 hours later, all were found to be greatly swollen. This condition was maintained for at least four days, but by the ninth day of immersion, all the corneas in the cold had dissolved.

7. Practical application

A practical application of the above results is apparent. Since cold so effectively retards dissolution of the cornea by alkali, it is evident that not only is continuous irrigation of the cornea with running water desirable, but that cold or ice water would aid in retarding the destructive action of the alkali on the corneal stroma. The application of cold to the eye for a period of hours after the initial irrigation therapy may prove to be of value in saving the remaining tissue.

8. Application of M/1 NaOH to the cornea of the living anesthetized rabbit

Small circles of filter paper, four-mm. in diameter, were soaked in M/1 NaOH and the excess caustic removed (Shapiro, 1955).

These were applied to the center of the cornea for periods varying from one to 60 seconds, after which the circle was washed away and the eye irrigated with running tap water for 14 minutes. Separation of the lids with a speculum during application of the agent prevented complication of the experiment by blinking and lacrimation. This technique results in a sharply localized burn area. The lids were closed with scotch tape, and the animal set aside for intervals from seven to 132 minutes, before killing the animal and preserving the eye. The eyes were prepared by the celloidin process, mainly; two excised corneas were run through paraffin (fig. 4-G and 4-J). Figure 4 shows a series of low-power photographs of corneal sections of such eyes, in which the burn duration varied from two to 60 seconds. Details regarding each section are contained in Table 1. The boundaries of the corneal area denuded of epithelium by the

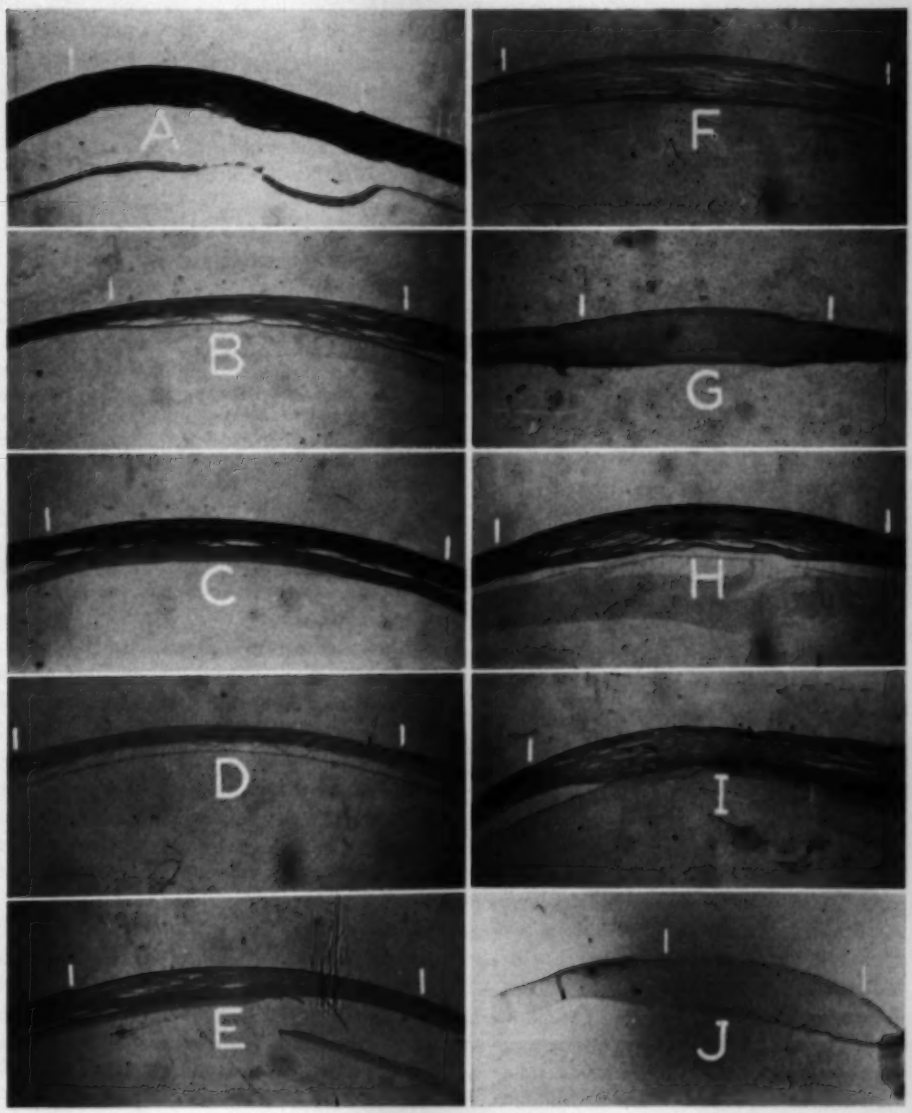

Fig. 4 (Shapiro). Low power views (×25) of corneas of anesthetized rabbits, in contact with M/1 NaOH from two to 60 seconds (A to J). Vertical white lines mark the boundaries of the cornea, denuded of epithelium. Note the greater swelling with longer exposure to alkali. In (A) the entire cornea (both burned and normal areas) is abnormally thick, apparently due to a technical aberrancy; yet the ratio (plotted in Figure 5) falls into its proper place on the curve.

TABLE 1

DETAILS OF PREPARATION OF SECTIONS SHOWN IN FIGURE 4

(All rabbits were adults, the burns were washed for 14 minutes after application of alkali, and fixed after the intervals indicated, in Bouin's fluid.)

Figure	Burn Duration (seconds)	Technique	Interval between Burn and Fixation (minutes)
4-A	2	Celloidin whole eye	90
4-B	4	Celloidin whole eye	41
4-C	7	Celloidin whole eye	26
4-D	9	Celloidin whole eye	58
4-E	11	Celloidin whole eye	42
4-F	17	Celloidin whole eye	73
4-G	30	Paraffin excised cornea	21
4-H	30	Celloidin whole eye	26
4-I	45	Celloidin whole eye	36
4-J	60	Paraffin, excised cornea	146

alkali are indicated by the white vertical lines. Figure 4-G is a section of an excised cornea after a 30-second burn, run through paraffin, whereas Figure 4-H is a section of another cornea, also burned for 30 seconds, in which the entire eye was processed in celloidin. Bands of fibrinous precipitate in the anterior chamber are visible in some of the photographs.

A control eye, to which no alkali was applied, showed no central swelling as a consequence of passage through the celloidin process alone. It is evident that the corneal epithelium is rapidly attacked and destroyed, and this is followed by destructive action of the alkali upon the subepithelial tissue, if longer contact is permitted. Taking the areas outside the vertical white lines in Figure 4, where the corneal thickness is approximately constant, as representative of normal cornea for any given eye, the thickness (exclusive of corneal epithelium) was compared with that of the maximally swollen central portion of cornea, within the white lines. Plotting the ratio of these two measurements, the curve in Figure 5 was obtained, with a minimal swelling observable, in histologic preparations, for brief burns of a few seconds. The swelling increased rapidly for burns of longer duration.

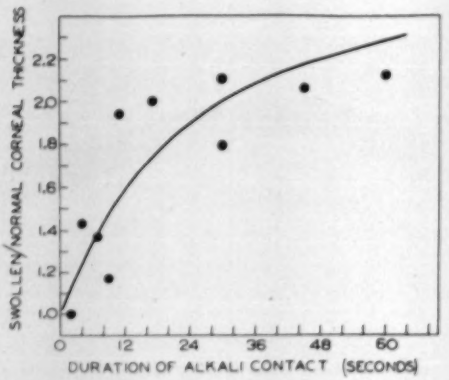

Fig. 5 (Shapiro). Ratio of maximal corneal swelling under alkali to normal corneal thickness, as a function of duration of exposure to alkali. Data obtained from measurements of the sections in Figure 4.

9. EFFECT OF THE FIXATIVE

A complicating factor is potentially present in the histologic interpretation and evaluation of swelling. This arises from the marked weight changes of tissues, which may occur in various fixatives (Shapiro and Harvey, 1955). In the present experiments it was noted that a corneal button allowed to swell in M/5 NaOH over a period of seven hours to a mass 413 percent the initial wet weight, when it attained to a weight of 174.4 mg., shrank after 38 minutes in Bouin's fluid to 131.4 mg., which was a loss of 24.7 percent. About 18 hours later

a slight further shrinkage occurred to 120 mg., or a total loss of 31.2 percent. A study of the behavior of normal rabbit cornea fixed in Bouin showed a shrinkage of only about 16 percent. If it is reasonable to extrapolate from these separate experiments, concerning the effect of Bouin fixative upon fully swollen and normal tissues, to the cases of the sections illustrated in Figure 4, it would seem that since the fixative shrinks both normal and burned areas of the experimental cornea, a qualitative but not a quantitative comparison with the original unfixed state is possible. This refers of course to mass alone. In other respects it is possible that a closer correlation exists.

Discussion

Corneal burns due to alkali are notorious for the severe injury produced in the eye (Duke-Elder) and are not uncommon owing to the widespread use of lye in industry and in the home. Ammonia burns have been stated to be the most serious of all the chemical burns (McAndrews). Sodium hydroxide has been found in the aqueous humor within five minutes after application to the eye (Berezinskaya).

Kinsey and Cogan have observed enormous swellings (up to 1,000 and 1,400 percent) in excised pieces of cat cornea immersed in solutions of K, Li, and $MgCl_2$. No correlation was observed with osmotic pressure, ionic valence, or nature of the ions. Each salt appeared to have its specific effect on degree of corneal turgidity produced. Distilled water and solutions of nonelectrolytes produced similar effects on corneal turgidity. Swelling occurred over practically the entire range of hydrogen-ion concentrations, from pH 1.0 to 14.0, and the isoelectric point for corneal turgidity was found at pH 4.3. Hart and Chandler established a swelling minimum for cattle corneas at pH 4.6, which they took as the apparent isoelectric point of the cornea.

Collagen is the protein present in highest concentration in the cornea, and on boiling breaks down into gelatin. The isoelectric point of gelatin is at pH 4.7. The swelling of gelatin in dilute acid or alkali was shown by J. Loeb to depend on the Donnan theory of membrane equilibrium. In the case of NaOH, the gelatin forms a sodium proteinate. The gelatin (protein) ion is fixed in the gel, and unable to diffuse away, with the result that a membrane equilibrium is set up. Since there is a greater concentration of osmotically active particles inside the gel than outside, water diffuses into the gel because of its higher osmotic pressure.

An apparently anomalous effect is mentioned by Loeb in that dry grains of isoelectric gelatin swell considerably when placed in water at pH 4.7. Since the gelatin is unionized, and the Donnan equilibrium is not set up, Loeb attributed the swelling of the solid isoelectric gelatin granules to a process of solid solution.

A buffering action of the cornea has been found by direct titration, using a glass electrode (Friedenwald, Hughes, and Herrmann). Since protein (mucoid, collagen, elastin, albumin, and globulin) is a significant constituent of the cornea (Hughes), this buffering effect is probably attributable in large part to the protein moiety.

Summary

1. Rabbit corneas in M/1 and M/5 alkali swell to approximately 400 percent their original mass. The course of swelling of the rabbit cornea in M/1 and M/5 NaOH at room temperature and in the cold was followed by weighing with a torsion balance.

2. At room temperature of approximately 30°C., swelling in M/1 NaOH reaches its peak in about four hours, and is followed by a rapid dissolution phase (fig. 1).

3. Corneas placed in cold M/1 NaOH require at least 20 times as much exposure to alkali in order to dissolve.

4. The initial swelling rate is high, being at room temperature about five percent per minute.

5. The mechanism of the weight increase

appears to occur through protein imbibition and vacuolization of the stroma, with accumulation of fluid in the vacuoles (fig. 2).

6. Brief localized application of alkali to the cornea of anesthetized rabbits resulted histologically in a swelling (fig. 4) whose magnitude bears a relationship to the duration of corneal contact with alkali (fig. 5).

7. A practical application of the above results in the case of alkali burns would be the immediate and continued irrigation of the burned cornea with cold water. The lower the water temperature, the more effective such a therapy presumably would be.

8. From measurements of histologic sections, in eyes to which M/1 alkali has been applied for periods varying from two to 60 seconds, the amount of swelling is a monotonic function of the duration of exposure (fig. 5).

5800 North Camac Street (41).

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ABSENCE OF SUPERIOR PALPEBRAL FOLD IN SLIT EYES*

An anatomic and physiologic explanation

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General consideration

Sappey[1] states that superior and inferior palpebral folds exactly superimposed the lines of reflection of the conjunctiva onto the globe (fornices). According to Charpey[2] they indicate the limit between the smooth and folded parts of that membrane. These authors do not explain, however, the absence of the superior palpebral folds in slit eyes.

Whitnall[3] states: "The superior palpebral fold is the deeper; it lies two or three mm. above the highest point of cutaneous insertion of the levator palpebrae superioris, the contraction of which muscle causes it to become deeply recessed; the orbicularis muscle is thinnest along this line. The skin of the orbital region of the lid above it often sags forward in middle age, when it has lost its elasticity, to form a fold ('Deckfalte') which covers the tarsal region even as low down as the eyelashes. It is most marked on the lateral side and may even form a kind of lateral epicanthus in old subjects."

According to my personal clinical observations, the superior palpebral fold even when the eyes are closed can be identified

* Read at the 10th anniversary celebration and scientific meeting of the Philippine Ophthalmological and Otolaryngological Society, November, 1955, at the Philippine General Hospital, Manila.

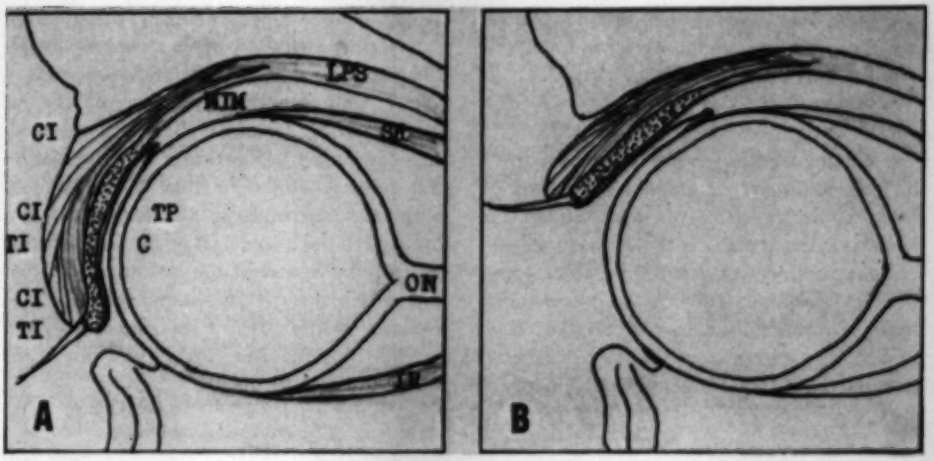

Fig. 1 (Sayoc). *Section of the eyelid with superior palpebral fold, showing cutaneous insertion of the terminal fibers of the levator palpebrae superioris. (A) Closed. (B) Opened.

*KEY

LPS—Levator palpebrae Superioris
ON—Optic nerve
IR—Inferior rectus
CI—Cutaneous insertion of the aponeurosis of the LPS
TP—Tarsal plate
SR—Superior rectus
TI—Tarsal insertion of the aponeurosis of LPS.
MIM—Müller's involuntary muscle.

by a cutaneous and somewhat horizontal line, which is produced and indicated by the highest cutaneous insertion of the terminal fibers of the superior levator muscle.

Anatomic basis

Review of the anatomy of the upper lid with special reference to the levator palpebrae superioris (Whitnall[3]):

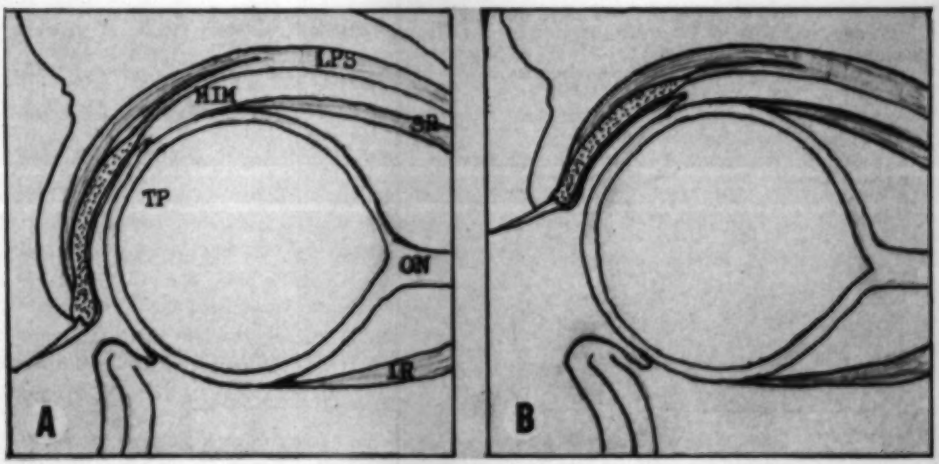

Fig. 2 (Sayoc). *Section of the eyelid in a slit eye, showing absence of the cutaneous insertion of the terminal fibers of the palpebrae superioris. (A) Closed. (B) Opened.

1. *Function.* Special elevator muscle of the upper lid lies in the orbit and only its terminal part enters the lid.

2. *Origin.* Arises at the apex of the orbit.

3. *Insertion.*

a. *Cutaneous* insertion is into the skin of the pretarsal part of the lid by means of the vertically radiating fibers of the delicate connective tissue: this is the primary and essential attachment of the muscle. In reaching the skin, the fibers traverse the horizontally disposed fasciculi of the orbicularis oculi muscle, then sweep over the bare superficial face of the tarsal plate in their downward course.

b. *Tarsal.* The lower fibers in their downward course are inserted into the lower third of the face of the tarsal plate and mingled with the bulbs of the cilia. The palpebral involuntary muscle (or Müller's) is inserted to the upper margin of the tarsal plate.

c. *Osseous.* Affected by the medial and lateral horns to the corresponding orbital margins at their mid-points and opposite the commisures of the lids.

Action of levator palpebrae superioris. By the contraction of the muscle belly of the special elevator of the upper eyelids, the transversely disposed aponeurosis is swung backward over the globe like a visor of a helmet, pulling with it the skin of the lid into which its terminal fibers are inserted, thus deepening and forming superior palpebral fold. At the same time the (1) tarsal plate is raised both by the terminal fibers attached to the lower part of its face and (2) the conjoint action of the involuntary palpebral muscle inserted into its margin, and (3) the loose conjunctiva of the superior fornix is pulled up by the fascial attachment of the levator muscle sheath.

Surgical findings

After having operated on over 200 slit or foldless eyes[4] and after having studied the anatomy of the upper lid and the anatomy and physiology of the levator palpebrae superioris in relation to the formation of the superior palpebral fold, I have observed that in slit eyes, the cutaneous insertion of the terminal fibers of the levator palpebral superioris is absent, which is an anatomic peculiarity common among orientals.

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NOTES, CASES, INSTRUMENTS

REMOVAL OF NONMAGNETIC FOREIGN BODIES*

FROM THE VITREOUS BY DIRECT VISUALIZATION

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The extraction of nonmagnetic foreign bodies from the vitreous while they are under observation with the ophthalmoscope is technically difficult.

A new method of removing foreign bodies by direct visualization has been successfully used in three cases. This method of viewing the fundus was first used by Coccius in 1853.[1]

A glass microscope slide with one end tapered to half its normal width is touched to the cornea with a drop of saline (fig. 1). The fluid fills the space between the glass surface and the convex cornea to neutralize its optical power. The interior of the globe can then be seen by simply looking in this window, provided it is well illuminated. The periphery is seen especially well by placing the glass slide on the side of the cornea.

The best illumination is provided by a binocular indirect ophthalmoscope worn on the head, as described by Dixon[2] and Schepens.[3] Thus the fundus can be seen with both eyes (fig. 2). The room should be dark and the observer's vision dark adapted. The fundus appears to be in miniature, but this is its normal appearance when not magnified. The forceps and foreign body within the vitreous are seen undistorted.

Thorpe vitreous forceps are passed through a sclerotomy opening at the pars plana. The resulting partial collapse of the globe does not disturb visibility but brings the periphery into better view. Grasping and removing the foreign body has not been difficult with this stereoscopic view. The first case attempted had a small foreign body adherent to connective tissue near the ora serrata. It was gently pinched away with the Thorpe BB-shot forceps without tearing the retina.

The foreign body should be clearly visualized by this method before attempting

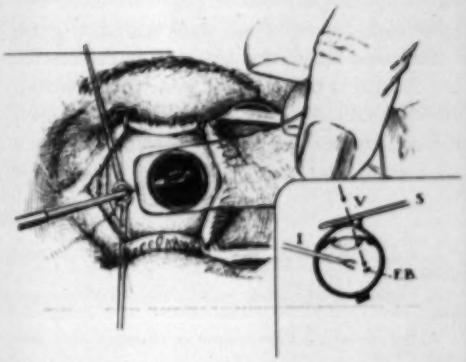

Fig. 1 (Dixon). View of forceps and foreign body through the pupil with microscope slide used as a contact glass. Lid sutures may be used instead of speculum. INSET: (S) Slide. (V) Line of vision. (I) Instrument. (F B) Foreign body.

Fig. 2 (Dixon). Use of indirect ophthalmoscope for stereoscopic view of the interior of the eye. Forceps must be introduced closed.

* From the Research Department of the Birmingham Baptist Hospital, and the Eye Pathology and Research Laboratory, Department of Ophthalmology, Medical College of Alabama. Supported by the Alabama Sight Conservation Service.

surgery and the pupil must be widely dilated. This method is also useful for quickly checking the positions of pins and diathermy punctures during retinal detachment surgery.

In some cases the lens is cataractous or the fundus is not seen for some other reason. In the excised pig's eye it has not been difficult to pass the forceps through the apex of a triangular flap in the pars plana while observing through the remainder of the opening with the glass slide in contact with the vitreous. During a personal discussion with Dr. Harvey Thorpe, he had this same idea. Brilliant illumination is necessary. Additional light may be passed through the pupil by a transilluminator held against the cornea.

2156 Highland Avenue South (5).

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THE ZEISS OPERATING MICROSCOPE*

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The availability of a stereoscopic operating microscope with excellent illumination and variable magnification offers attractive possibilities for use in ophthalmic surgery. This instrument is similar in design to the familiar Zeiss slitlamp with easily changed parfocal magnifications (X6, X10, X16, X25, and X40). It can be moved to any desired position by means of the joints and swinging arm, and the light and field are focused accurately by a single knob. Since this instrument does not appear to be in general use in eye operating rooms, it appears worthwhile to call it to the attention of ophthalmologists.

The operating microscope has been available in the McMillan Hospital during the past 25 months and has proved most useful in a number of examinations and procedures.

For examination of infants and children under anesthesia, the operating microscope provides the excellent magnification of the slitlamp. Careful observations can be carried out on lens opacities, capsular remains, intraocular and corneal foreign bodies, injuries, and lacerations. Gonioscopy can be readily performed in both children and adults

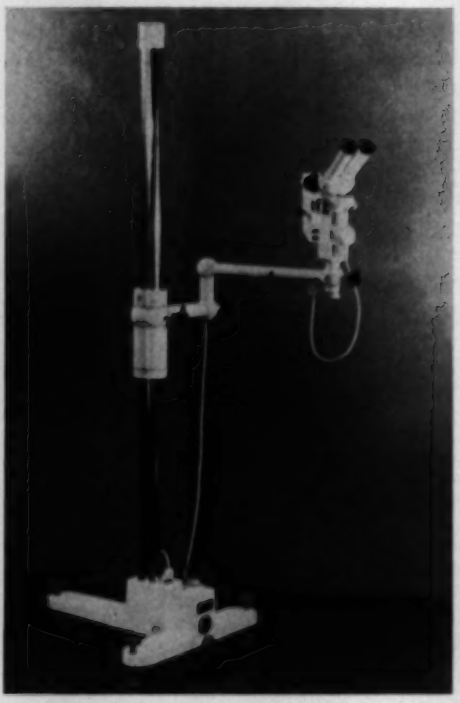

Fig. 1 (Becker). The Zeiss operating microscope.

* From the Department of Ophthalmology and the Oscar Johnson Institute of the Washington University School of Medicine.

under variable magnification with excellent illumination and with one hand free for manipulation of the eye and prism or lens.

The principal surgical uses of the instrument have been for goniotomies, discissions, corneal transplants, repair of lacerations, and removal of foreign bodies. The long working distance which is the same for all magnifications affords ease of surgical manipulation. The use of a sterile "sleeve" for the microscope permits focusing and changing of position and magnification without danger of contamination.

Goniotomy can be performed under direct visualization without the need for assistants to hold the light source or the eye. Discissions of congenital cataract or capsular remains can be carried out precisely under stereoscopic observation with magnifications of X16 or X25. The use of the instrument in routine cataract extraction has proved disappointing thus far because of the limited visual field and awkwardness of grosser movements. However, the inspection of suture placement, of adequacy of wound closure, of the anterior chamber, and of the status of the corneal endothelium toward the close of the procedure have proved most instructive. The direct suturing of corneal transplants under magnification permits much more precise approximation of edges. In lamellar grafts the preparation of a smooth bed with removal of all possible opacity and with perpendicular and regular edges is greatly facilitated. The direct suturing of corneal and corneoscleral lacerations as well as secondary wound closures can be accomplished with greater precision. Removal of corneal, scleral, and anterior chamber foreign bodies is made much easier under direct observation.

In the laboratory the instrument proves most useful in the gross and semimicroscopic examination of enucleated eyes. It is also of enormous aid in carrying out various operative procedures, cannulations, and dissections of the eyes of the smaller laboratory animals.

The availability of a new photographic attachment* with an electronic flash offers additional attractive opportunities for recording observations and surgical procedures.

From the above summary it is apparent that the Zeiss operating microscope is an instrument that warrants further trial and more attention from ophthalmologists.

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CORNEAL ULCER DUE TO NOCARDIA ASTEROIDES

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AND
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Fungus infections of the eye, though not rare, are not frequently reported. Birge[1] has reviewed the literature thoroughly. Recently Pantler, Roberts, and Beamer[2] reported a corneal ulcer due to Monosporium apiosermum. Nocardia infection of the eyeball is rare. Benedict and Iverson[3] reported a case of chronic keratoconjunctivitis in a 23-year-old woman who had bilateral involvement with flare-ups lasting one to seven weeks with relatively quiet episodes, since she was seven years of age. The inner surfaces of the eyelids presented large patches of granulation and scar tissue. The right cornea was involved throughout with an interstitial keratitis with vascularization of all parts of the cornea. The left cornea was approximately normal. No treatment was of benefit. Eight cultures over a four-year period showed nocardia with other organisms. Both living and dead organisms injected into a rabbits cornea caused only a foreign-body reaction.

The order actinomycetales[4] is divided into three families: (1) Mycobacteriaceae, (2) Actinomycetaceae, (3) Streptomycetaceae. The genera nocardia and actinomyces belong

* Littmann, H.: A new photographic device. Photographie und Forschung, 6:3 (Apr.) 1954.

to the second family. The laboratory diagnosis is made by culturing on ordinary laboratory media in nocardial infection. All nocardia are gram positive; some are acid fast; they are aerobic. They produce branching mycelium, no spirals, are segmented to bacillary and coccoid forms. They have an earthy odor.

Disease in man and animals caused by the nocardia is called nocardosis. Nocardia asteroides is the most commonly involved organism. Most of the nocardias have been isolated from the soil. Clinically[5] nocardosis resembles tuberculosis and usually occurs in workers in the soil. There are three usual types of infections (1) mycetoma, a localized unilateral infection usually in the extremities; (2) pulmonary, resembling tuberculosis; and (3) systemic, probably pulmonary in origin with metastases throughout the body.

Report of case

A 33-year-old white man was first seen in the office complaining of pain, tearing, and discharge from the right eye of three weeks' duration. The patient was struck in the right eye by a stone while working in a farmyard and the only treatment was 20-percent argyrol for the three previous weeks.

The office examination revealed the vision in the right eye to be 20/100. The eye was red with some swelling of the lids. There was a large dirty corneal ulceration with overhanging edges about three mm. in diameter extending from the limbus at the inferior temporal aspect. There was a two-plus flare with cells in the anterior chamber. The patient was treated by cauterization with iodine neutralized with cocaine, atropine (one percent), terramycin ointment, and patching.

The disease followed a chronic course with marked photophobia and an increase in the size of the ulcer with undermined necrotic edges. At times, the ulcer appeared to be healing only to break down and become more extensive. Never did the ulcer become deeper than one quarter of the thickness of the cornea.

Three weeks later a culture on blood agar showed no growth after 48 hours. In addition to the local antibiotics and ointments, oral terramycin (250 mg. four times a day) had no effect in healing the ulcer. Finally, a second culture taken two weeks later showed no growth in 48 hours but did show an actinomycotic organism after 72 hours, identified by Mr. C. V. Hayes, bacteriologist at the Hartford Hospital, as Nocardia asteroides. It was found to be most sensitive to Achromycin. This was confirmed by Leanor D. Haley, director, Microbiologic Laboratories, Yale School of Medicine. A repeat culture was taken several days later with Nocardia asteroides again reported.

Inoculation of the corneal epithelium and stroma of two rabbits failed to produce more than a traumatic reaction and healed promptly. When inoculated into mice, a granulomatous type of infection developed, involving diaphragm, spleen, mesenteric, and kidneys. Guinea pigs were inoculated; one failed to develop any lesion; the second, however, died seven days after inoculation and, when autopsied, revealed the same type of pathologic process as seen in the mice. Bacterial antibiotic sensitivity tests showed some penicillin sensitivity, extreme sensitivity to achromycin, and slight sensitivity to erythromycin. It was not sensitive to dihydrostreptomycin, chloromycetin, aureomycin, or terramycin.

The patient was hospitalized and given achromycin (250 mg. orally every six hours) for one week with local achromycin ophthalmic ointment. He showed marked improvement and the ulcer healed rapidly. While in the hospital, the blood count, urine analysis, chest X-ray examination, and sedimentation rate were normal. The patient was kept on the achromycin, both orally and locally, for two weeks after discharge. When the patient was last seen, he was entirely asymptomatic except for blurred vision due to corneal scarring. The vision was 20/80

and the scar which covered the temporal half of the cornea was thinning out. The eye was quiet and there was no corneal staining. The patient has gone back to work.

Conclusion

This case points out the need for cultures in corneal ulcers which do not respond readily to routine antibiotic therapy. One should also recognize the fact that, if there is no growth at the end of 48 hours, the culture should not be discarded, since some of the etiologic organisms require 72 to 96 hours to produce a growth.

935 Main Street.

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PHTHIRIASIS PALPEBRARUM

A case report

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Phthiriasis palpebrarum is that condition in which the crab-louse (Phthirus pubis) involves the eyelashes. In adults the parasite probably reaches the margins of the eyes by transmission by the hand from the pubic hair and, in this way, one eye only may be affected. In children head-to-head transmission may be the most likely mechanism. Although the louse, or several of them, may be found attached to the lashes or brows, it is usually the presence of nits on the lashes that first suggests the diagnosis of phthiriasis. Because of its infrequent occurrence in the United States, the following case report is submitted.

Case report

The patient, a 25-year-old, right-handed white man, was examined by me on October 26, 1955. The presenting complaint was that of intense itching and marked redness of the right eye. These symptoms had been present for approximately three weeks and, during that period, the patient was aware of generalized pruritus when he went to bed at night.

Examination revealed a marked blepharoconjunctivitis with pronounced folliculosis in the right eye. There was a mild nonulcerative blepharitis of the left eye. Under the slitlamp, a distinct blackish ovoid particle was seen attached near the base of the convex aspect of each lash of the right upper lid. Only the usual flat yellowish-white crusts characteristic of nonulcerative blepharitis were evident on the lashes of the left eye.

An attempt was made to remove some of the nits by means of vigorous brushing with a toothpick swab. This was of no avail. On re-examination with the slitlamp, however, it was evident that several opercula had been removed by this maneuver, for several of the nits remained as hollow shells. In addition adult forms were now seen clinging to the base of several lashes. Examination of the rest of the body revealed scratch marks in the pubic, pectoral, and axillary regions. No adult forms were found in these regions. The scalp did not appear grossly infested.

The following treatment was carried out in the office:

Eserine eye ointment (0.25 percent) was rubbed into the lash border with a toothpick swab. Cilia forceps were then applied

to each lash of the upper lid and the nit of each lash was slid along from the base to the tip of the lash and thus removed. This procedure was carried out until examination under the slitlamp revealed that all the nits had been removed. The patient was instructed to massage eserine eye ointment into the lid margins twice daily and to apply a lotion consisting of DDT and benzyl benzoate to the scalp and remainder of his body. He was also advised to instill one drop of Terra-Cortril ophthalmic suspension into the conjunctival sac every two hours while he was awake.

When the patient returned for follow-up evaluation five days later, the eyes appeared perfectly normal. All ocular and general symptoms attributable to the infestation with lice had completely disappeared.

Summary

A case of unilateral phthiriasis palpebrarum has been presented. Effective treatment consisted of the manual removal of all nits from involved lashes together with generalized treatment—of the scalp, the pubic area, and the remainder of the body—with DDT and benzyl benzoate. Eserine eye ointment was utilized as originally suggested by Cogan.*

277 Alexander Street.

* Cogan, D. G., and Grant, W.: Treatment of pediculosis ciliaris with anticholinesterase agents. Arch. Ophth., **41**:627-628, 1949.

CORNEOSCLERAL SUTURING FORCEPS

HARRY GOLDBERG, M.D., AND BERNARD GOLDBERG, M.D.
Jamaica, New York

In suturing fine tissues, such as the cornea, it is important that trauma is minimized and accuracy of placement is maximum. In tissues grasped at one point with present corneal suturing forceps, there is a tendency to drag on the cornea when inserting the needle, with consequent damage to the cornea. However, if the tissue to be sutured (cornea or sclera, or both) is fixed at two points, there is much less probability of bending or lacerating the cornea, and the grasp on the cornea can be lessened.

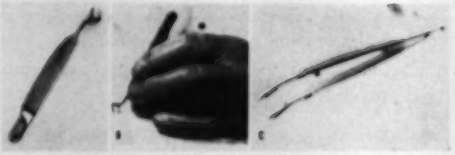

Fig. 1. (Goldberg and Goldberg). Corneoscleral suturing forceps.

The forceps we are presenting allows this to be done. The head of the forceps has two sets of teeth two mm. apart. It is a two (bottom) to one (top) arrangement, being pointed obliquely out at 45 degrees. The teeth are fine (0.5 mm.) and sharp (fig. 1-A). The neck and shaft have a curvature of about 10 degrees so that the operator's hand can be held in a comfortable position while grasping the cornea, that is, it does not have to be in the same horizontal plane as the edge of the cornea (fig. 1-B and C). There is an angle between the head and the shaft of about 120 degrees so that when the operator holds the forceps the view of the tissue, needle, and holder is not obstructed. The posterior portion of the head is wider than the anterior portion where the teeth are located to give the operator more room to maneuver the needle holder and needle (fig. 1-B). There are two stops to prevent excessive pressure in grasping the cornea or sclera (fig. 1-C).

These forceps can also be used in traumatic lid repairs and plastic procedures to minimize trauma to fine lacerated skin edges.

88-02 150 Street (35).

OPHTHALMIC RESEARCH

EDITED BY FRANK W. NEWELL, M.D.

Research program for the fiscal year, 1956, of the
NATIONAL INSTITUTE OF NEUROLOGICAL DISEASES AND BLINDNESS

The total program of the Institute, including all intramural basic and clinical projects and the extramural program of grants-in-aid, totals 558 projects in the amount of $7,664,900. Research in diseases of the eye total 110 projects in the amount of $1,461,500.

RESEARCH IN DISEASES OF THE EYE

	PROJECTS	FUNDS
1. Cataract	13	$165,100
2. Glaucoma	16	261,500
3. Retinopathy	16	245,100
4. Retrolental fibroplasia	5	63,100
5. Inflammatory diseases	14	206,100
6. General	24	200,600
7. Strabismus	4	41,000
8. Other	18	279,000
	110	$1,461,500

RESEARCH PROJECTS SUPPORTED OR COMMITTED FOR SUPPORT

(OPHTHALMOLOGY)

INVESTIGATOR AND INSTITUTION	PROJECT TITLE	1956
Stephen W. Kuffler Johns Hopkins University	Physiology of the visual system	$18,486
Leon S. Stone Yale University	Regeneration of lens, iris and retina	10,648
Lorand V. Johnson Western Reserve University	Nutrition, metabolism avascular structures of eye	10,524
Alfred E. Maumenee Johns Hopkins University	Study of the etiology and treatment of uveitis	13,340
Michael J. Hogan University of California at San Francisco	Investigation on ocular toxoplasmosis	9,974
I. H. Leopold Wills Eye Hospital	Corticosteroids in the aqueous humor	14,000
Arnall Patz Georgetown University	Studies in retrolental fibroplasia	16,644
W. Morton Grant Harvard College	Actions of chemicals injurious to eye	11,661
Randall Wm. Reyer University of Pittsburgh	Lens induction and lens regeneration	4,046
Elmer J. Ballintine Western Reserve University	Secretory mechanisms of the ciliary body	20,230
Aeleta N. Barber Louisiana State University	Development of the human visual pathway	4,472
Alfred E. Maumenee Johns Hopkins University	Study of diabetic retinopathy	19,166
Chih Chiang Teng Eye-Bank for Sight restoration	Anatomic study of the retinal periphery	10,000
K. W. Ascher University of Cincinnati	Aqueous-veins research	7,986
Michael J. Hogan University of California	Action of lytic enzymes on eye structures	10,879
John E. Harris University of Oregon	Cations and hydration of the cornea and lens	10,642
Charles I. Thomas Western Reserve University	Application of radioactive isotopes to the eye	12,777
R. Winston Roberts Bowman Gray School of Medicine	Glaucoma study	3,726
W. Morton Grant Massachusetts Eye and Ear Infirmary	Study of pressure-regulating mechanisms in glaucoma	14,030
Ralph G. Janes State University of Iowa	Ocular changes in diabetic animals	7,219
James C. Peskin University of Rochester	Carotenoid and protein in the visual receptor system	4,549
Otto Lowenstein College of Physicians and Surgeons	Autonomous nervous system of pupillography	13,800
John G. Linn, Jr. University of Pittsburgh	Development of diabetic retinopathy	4,060
Albert C. Snell, Jr. University of Rochester	Reactions of the iris to injury	6,131
Endre A. Balazs Retina Foundation	The state of hyaluronic acid in the vitreous body	15,735
James H. Allen Tulane University	Ocular involvement in visceral larva migrans	9,000
Hermann M. Burian State University of Iowa	Electrical responses of human visual system	16,546
Donald B. Lindsley University of California	Mechanism of vision in man and animal	17,037
Alfred E. Maumenee Johns Hopkins University	Enzymatic histochemical studies	9,343
Jerome J. Wolken University of Pittsburgh	Photoreceptor structures in biological systems	8,578
Oliver H. Lowry Washington University	Quantitative histochemistry of the retina	6,175
Marie A. Jakus Retina Foundation	Fine structure and properties of the fibrous components of the eye	14,664
James L. Wilson University of Michigan	Plasma oxygen tension in infants	5,324
S. Rodman Irvine University of California	Surgery of detached retina	11,996
K. Scharenberg University of Michigan	Investigation of the human eye with the silver carbonate method	8,050
George K. Smelser Columbia University	Differentiation of ocular tissues	10,240
Jack H. Prince Ohio State University	Visual screening tests	2,070
H. V. Platou Southern Eye Bank	Co-operative study on retrolental fibroplasia	20,268
Alexander Forbes Harvard University	Response of vertebrate retina to color shift	3,500
Frederick Crescitelli University of California, Los Angeles	A comparative study of retinal pigments	2,998
Hunter H. Romaine New York Eye and Ear Infirmary	B. subtilis and related organisms as eye pathogens	10,143
George Wald Harvard University	Chemistry of rod vision	7,113
A. Leonard Diamond Northwestern University	Simultaneous brightness contrast	5,807
Arthur M. Culler Ohio State University	Immunology of uveitis	5,796
Ernest Jawetz University of California	Studies of viral keratoconjunctivitis	20,366
Bernard Becker Washington University	Rate of flow of aqueous humor in the rabbit eye	24,490
Robert M. Boynton University of Rochester	Chromatic adaptation and stray light in vision	12,588

Investigator and Institution	Project Title	1956
Wendell D. Gingrich University of Texas	Irradiation of the ciliary body of the eye	5,290
Charles L. Schepens Massachusetts Eye and Ear Infirmary	Improvements in the diagnosis of uveitis	13,800
Merrill J. King Massachusetts Eye and Ear Infirmary	Study of mild and severe retrolental fibroplasia	14,375
Philip B. Armstrong Marine Biological Laboratory	Encephalization in embryonic development	2,012
John G. Sinclair University of Texas	Mechanism of the iris and ciliary body	5,657
Arthur Jampolsky Stanford University	Investigation of ocular divergence mechanisms	5,146
J. W. Bettman Stanford University	Vasodilator and vasoconstrictor drugs on intraocular circulation	3,705
Harry Green Wills Eye Hospital	Investigation of lens metabolism	10,292
Samuel Kaplan Children's Hospital Research Foundation	Polarographic measurement of oxygen tension in infants	6,497
David G. Fleming University of Kansas	Vascular factors in visual accommodation	4,255
Henry Dolger Mount Sinai Hospital	Diabetic retinopathy and vitamin B_{12}	8,395
Ludvig G. Browman Montana State University	Blood supply in embryos of microphthalmic rats	3,000
J. R. Couch University of Texas	Vitamin E and the embryonic development of the eye	7,465
Kay T. Rogers Oberlin College	Research in neuroembryology	1,064
Austin H. Riesen University of Chicago	Co-ordinated fixation and convergence movements	6,921
Austin H. Riesen University of Chicago	Retinal atrophy after light deprivation	6,981
Algernon B. Reese Columbia University	Cytology and biochemistry of human pigmented ocular tissue	11,712
Arnold Lazarow University of Minnesota	A study of diabetic retinopathy	21,296
J. Francis Hartmann University of Minnesota	Studies of the central nervous system	12,241
William van Herick University of California	Studies on ocular toxoplasmosis	9,372
John R. Harrison Miami University	Growth and differentiation of the chick embryo eye	2,242
Frank W. Newell University of Chicago	Nystagmus	2,875
William John Nelson Department of Health Territory of Hawaii	Prevention and treatment of ocular leprosy	4,700
Werner K. Noell Health Research, Inc. Buffalo, New York	Metabolic and functional development of the retina	14,204
T. F. Schlaegel, Jr. Indiana University	Emotional factors in uveitis and glaucoma patients	9,038
George Wald Harvard University	Mechanisms of cone and color vision	7,666
S. Rodman Irvine University of California, Los Angeles	Hyaluronic acid-hyaluronidase balance in ocular tissue	16,644
Wood Lyda University of Washington	Endophthalmitis phacoanaphylactica	5,750
Haldon H. Hartline Rockefeller Institute	Electrical activity of single receptors and neurones of the eye	17,206
George Clark University of Buffalo	The neural basis for flicker phenomena in the cat	5,853
Alfred J. Coulombre Yale University	Intraocular pressure in growth of vertebrate eye	5,290
S. C. Culbertson South Bend Medical Foundation	Toxoplasma gondii in etiology of retinochoroiditis	5,692
Milton Flocks Stanford University	Physiology and anatomy of trabecular meshwork	13,961
Aeleta N. Barber Louisiana State University	Congenital blindness	7,989
Gertrude Rand Columbia University	Electroretinogram and flicker fusion	13,468
Ronan O'Rahilly Wayne University	Histological and histochemical studies in ophthalmic developments	6,727
Lazlo Varga Retina Foundation	Studies on mechanical properties of biologically important gels	15,987
Goodwin M. Breinin New York University-Bellevue	Electromyography of the extraocular muscles	18,487
Ward C. Halstead University of Chicago	Factors in mental development of young blind children	21,907
Robert W. Doty University of Utah	Physiological study of visual cortex	10,630
H. Richard Blackwell University of Michigan	Electrophysiology of color vision	12,305
Gilbert Baum New York University-Bellevue	Application of ultrasonic locating to ophthalmology	18,408
Adolph W. Vogel Wills Eye Hospital	Intralenticular implantation of various compounds	5,900
Robert B. Livingston University of California	Central co-ordination of eye movements	20,993
Seymour P. Halbert Columbia University	Immunologic observations on ocular lens in cataract	11,270
Frederick C. Goetz University of Minnesota	Clinical and physiologic studies of diabetes patients	9,200

Ophthalmic Miniature

Another good feature of the extended conjunctival flap (in cataract surgery) was that it usually covered any point of defective healing of the wound occasioned by incarcerated tags of iris. Thus there was no opportunity for downgrowth of epithelium into the anterior chamber—one of the serious causes of secondary glaucoma.

H. Herbert,
Tr. Ophth. Soc. U. Kingdom, 34:45, 1914.

SOCIETY PROCEEDINGS

Edited by DONALD J. LYLE, M.D.

CHICAGO OPHTHALMOLOGICAL SOCIETY

March 21, 1955

DR. JUSTIN DONEGAN, *President*

The Suker Memorial Clinic was held at Cook County Hospital at 4:00 P.M.

OCULAR EFFECTS OF Co^{60} BODY IRRADIATION

Capt. David V. L. Brown, Dr. Paul A. Cibis, and Col. J. E. Pickering presented a paper on the "Ocular effects following head, body, or whole body exposure to Co^{60} gamma rays." This is part of a very large-scale study of the effects of irradiation on mammals. The authors point out that the effects of ionizing radiation on the crystalline lens have received intensive study in the past decade; however, radiation studies on the retina have not been emphasized.

In an earlier investigation Co^{60} gamma radiation was delivered to the head region of young adult monkeys. Pyknosis of the visual cells occurred with doses as low as 2,000 r; however, no attempt was made to establish a time threshold for the appearance of retinal abnormalities.

It was the purpose of the present paper to describe the retinal changes found in a study of 48 young adult male Macaca rhesus monkeys which had been exposed to massive doses of Co^{60} gamma radiation delivered at a high dose rate. The authors' aim in this investigation was the determination of a time threshold for pyknosis of visual cells following a single dose of ionizing radiation, and also to ascertain whether this was a direct radiation effect

Fixed doses of 10,000 r were delivered at a rate of $1,000 \pm 50$ r/minute either to the head (body shielded); to the body (head shielded); or to the entire body including the head. Two animals from each group were then killed by decapitation at 2, 4, 8, 12, 24, 48, 72, and 96 hours after radiation.

Ocular abnormalities were found only in those animals which received radiation directly to the eyes.

Changes seen in the eyes of animals exposed to head radiation were essentially similar to those changes seen in the monkeys receiving whole-body radiation. Clinical manifestations consisted of severe iridocyclitis, retinal edema, papilledema, severe ocular hypotony, and, in a few cases, punctate and flame-shaped retinal hemorrhages.

Histologic abnormalities consisted chiefly of pyknosis of rod nuclei (apparent as early as two hours following radiation) and degenerative sequellae in the outer nuclear and bacillary layers.

Both clinical and histologic alterations developed in a definite time pattern.

Discussion. DR. WILLIAM F. HUGHES, JR.: This very interesting paper is the first work I have heard on acute radiational changes in the retina. I would like to ask how the dosage and effect on the rods compares with the epithelium and connective tissue change. Could the change be secondary to damage to circulation and vascular supply to the retina?

DR. D. V. L. BROWN (closing): Doses of this level are of course uniformly fatal. We have no such findings in doses which are of a sublethal nature. We have several experiments in progress on radiation cataracts employing lower doses. However, none of these animals are dying, and we want to follow them for a long time. As to endothelial and connective-tissue changes, the retinal vessels are less sensitive. Dosage of 250 r can cause an almost immediate transient change in the permeability of the anterior uveal vessels. We know we have massive choroidal hemorrhage if the animal lives for two or three weeks.

PERFORATING CORNEOSCLERAL INJURIES

DR. IRA ABRAHAMSON, JR., DR. HOWARD LIEBERMAN, DR. RIMVYDAS SIDRYS, AND DR. THEODORE ZEKMAN presented a statistical survey of 292 cases of perforating corneoscleral injuries admitted to Cook County Hospital in the seven-year period from 1947 through 1953. Although many different factors affect the prognosis in any case, the authors felt that in general good initial visual acuity was a favorable sign, since it indicated an intact macula and probably retina. Injuries limited to the cornea also carried a good prognosis in contrast to scleral and limbal wounds which were usually associated with more severe intraocular injury. Surprisingly enough the most serious injuries were those resulting from blunt force rather than from sharp penetrating injuries.

Discussion. DR. W. F. MONCRIEFF referred to his paper on this subject (THE JOURNAL, **36**:375, 1953). He felt that in spite of improved systemic therapy and variations in surgical technique, the figures given here were in good agreement with previous data. In series of this size and with the number of variables present, statistical analysis is likely to be misleading. He felt that the only conclusion it was absolutely safe to draw was that the final outcome was dependent on the original severity of the injury.

DAVID SHOCH,
Recording Secretary.

YALE CLINICAL CONFERENCE

April 29, 1955

DR. R. M. FASANELLA, *presiding*

MODERN TRENDS IN CORNEAL TRANSPLANTATION

DR. RAMON CASTROVIEJO (New York) noted in introduction that the most important consideration in this subject is to develop clinical and surgical judgment, rather than the details of the operation itself. He pointed out the value of work on large numbers of cases in developing this type of judgment. In studying the indications for various methods of treatment, one cannot separate the use of keratectomy and keratoplasty from associated plastic surgery, such as the treatment of the symblepharon and other associated abnormalities. It is now known that, in corneal transplantation, only homotransplants or autotransplants are successful. The donor can be any eye with a good cornea. An eye excised for tumor, glaucoma, or a cadaver eye can be preserved in a humid chamber for three or four days. A newborn eye is good only if the child is full term.

Dr. Castroviejo then presented by means of numerous slides and discussion of cases, the various conditions that require surgery, ranging from the simplest type of lamellar keratectomy to the more complicated types of total penetrating keratoplasty. The question of corneal and pericorneal vascularization was discussed. It is well known that these cases do poorly in corneal transplantation. Too much radiation preoperatively is definitely unfavorable. Dr. Castroviejo much prefers doing a keratectomy followed by beta irradiation at the limbus after surgery.

Procedures such as keratectomy or keratoplasty often have to be combined with plastic repair of symblepharon and reconstruction of the fornix. Material dissected from the cornea can be used, supplemented by buccal mucous membrane grafts. Several indications were shown for each type of operative procedure. A partial lamellar keratoplasty was used for a central superficial opacity. In a case of corneal lipoid dystrophy, an almost total lamellar keratoplasty was thought to be better than a small penetrating keratoplasty which might again develop dystrophy.

A partial penetrating keratoplasty is useful for a deep central corneal opacity. Groenouw's dystrophy responds well to this type

of procedure. It is also often used in cases of interstitial keratitis.

For the treatment of the vascularization, one can do a peritomy and apply 1,500 to 2,500 r of radiation postoperatively. Cases of Fuchs' epithelial dystrophy are best operated on when the lesion is still central. When the whole cornea becomes involved, the prognosis is much poorer.

In keratoconus the entire keratoconus must be removed. A square transplant in this case is often better, as it allows a smaller graft. When the corneal transplant becomes cloudy postoperatively, the reasons may be (1) faulty healing, (2) anterior synechias, or (3) uveitis associated with upper respiratory infections.

As long as the cornea is bloodless with a healthy peripheral cornea, reoperation is feasible. Operation in one case while under treatment with 150 mg. of cortisone daily showed no failure of healing. Some cases were presented in which a third or even a fifth corneal transplant operation was successful, when previous transplants did not remain transparent. In keratoconus a small graft may be transparent, but if the entire keratoconus is not removed, the essential condition still persists and vision is distorted.

In summary three graded types of corneal treatment were mentioned:

1. Lamellar keratectomy, partial or total.
2. Lamellar keratoplasty, partial or total.
3. Penetrating keratoplasty, partial or total.

Each of these combined with various plastic procedures of the lids and fornix. Dr. Castroviejo then showed a movie demonstrating various procedures.

Discussion. DR. FASANELLA: Do you use frozen grafts?

DR. CASTROVIEJO: So far my animal experiments have not been encouraging enough to let me use them on humans. The use of glycerinated dehydrated material is also interesting.

DR. GLASS: How soon after keratoplasty can irradiation be started?

DR. CASTROVIEJO: Immediately at the end of the operation, if vascularization is already there.

DR. FASANELLA: If you had an anterior synechia, would you treat it at operation?

DR. CASTROVIEJO: If there were a few synechias, the condition could be treated at operation. If extensive, it should be treated beforehand.

DR. FASANELLA: Do you use drops?

DR. CASTROVIEJO: Generally nothing is used. However, with a small graft, I may use atropine to prevent adhesions of the iris.

DR. FASANELLA: When would you treat postoperative adhesions?

DR. CASTROVIEJO: After two weeks; possibly during the third or fourth postoperative weeks. I remove the corneal sutures usually on the 11th day, with akinesia and local anesthesia.

DR. WIES: Do you use any instrument to protect the lens?

DR. CASTROVIEJO: No. A prophylactic spatula is no longer used.

DR. KAPLAN: How do you handle a case with a combined cataract and corneal transplant?

DR. CASTROVIEJO: I do the transplant first then the cataract six months later, waiting until the new membrane covers the gap. The usual routine cataract operation is used.

DR. FASANELLA: Do you use peritoneum?

DR. CASTROVIEJO: Yes, but it doesn't behave as well as a mucous membrane graft if you make this thin enough.

DR. WONG: Do you ever do a combined transplantation and cataract operation?

DR. CASTROVIEJO: Only in cases with very large grafts, and here I always do a large iridectomy to prevent postoperative glaucoma which still happens fairly often.

DR. FASANELLA: Following lye burns, how long would you wait for corneal transplantation?

DR. CASTROVIEJO: Until the eye is completely quiet. Six months at least, preferably one year.

During the discussion Dr. Castroviejo

noted that the two most important instruments for the corneal transplant operation are a sharp needle and good forceps and he feels they should not be considered accessories, but main instruments. He has done grafts on children of six months and on unruly patients and, as long as multiple edge-to-edge sutures are used, he does not worry about this type of patient.

DR. FASANELLA: Will you bring us up to date on your feelings on cyclodiathermy in the treatment of glaucoma?

DR. CASTROVIEJO: I think it is a great addition to our useful operations. One must remember that you cannot go backward in this type of operation if you do too much at one sitting. Therefore, if you doubt about how much to do, do too little rather than too much. I now place applications about six mm. behind the limbus. When the tension is 35 to 40 mm. Hg or more, I do three applications per quadrant making a total of 12 in all to start with. I used to do four applications per quadrant, but I feel that a total of 12 is safer to start with. If the tension can be controlled to 25 or 26 mm. Hg with drops but the patient is losing field, do two applications per quadrant. If the tension is not maintained at normal level six to eight weeks later, you may do one more application per quadrant. If further treatment is necessary, two applications at a time for subsequent procedures. Operation is done under retrobulbar anesthesia using four cc. of Xylocaine (two percent) plus hyaluronidase plus massage, waiting for five minutes before starting the procedure. It is not advisable to inject the conjunctiva, in order to localize the spread of current as much as possible. Dry the area well before each application. Postoperatively no medication is used. The next day pilocarpine might be used. If there is too much reaction, medication should be stopped. If the eye is soft, only antibiotics should be used.

DR. GLASS: How long after operation can you evaluate your results?

DR. CASTROVIEJO: You should wait two to three months before reoperation. One should control the patient with Diamox and cortisone to control the temporary secondary rise in tension due to an irritative reaction.

DR. GLASS: Have you used cyclodiathermy in congenital glaucoma?

DR. CASTROVIEJO: Yes, but in this case where the eye is very large, one must go a little further back from the limbus.

DR. GLASS: Do you use cyclodiathermy in so-called low-tension glaucoma?

DR. CASTROVIEJO: In a patient with a tension of 26 mm. Hg or over and a loss of field, I would use it. To my mind this does not represent a normal tension for that person. If the tension is already 15 to 18 mm. Hg, I do not feel this is a glaucoma.

WILLIAM I. GLASS,
Recording Secretary.

COLLEGE OF PHYSICIANS OF PHILADELPHIA

SECTION ON OPHTHALMOLOGY

February 17, 1955

DR. EDMUND B. SPAETH, *Chairman*

OCULAR TOXOPLASMOSIS

DR. MICHAEL J. HOGAN (San Francisco) presented aspects of the clinical and laboratory findings in congenital and acquired ocular toxoplasmosis.

Congenital toxoplasmosis is associated with a chorioretinitis in 80 percent of cases. One or both eyes may be affected, and single or multiple lesions may develop. The acute inflammation may be present prior to birth, at birth, or develop in the neonatal period. Occasional patients develop the initial ocular inflammation any time within the first year after birth. Several courses may be followed by these patients:

1. Complete quiescence, after healing, throughout the patient's life.

2. Relapse of a previously healed chori-

oretinitis as long as four to 25 years after the initial disease.

The diagnosis of acute cases in the newborn presents no difficulty. A combination of central nervous system disease, visceral disease, and chorioretinitis, along with a positive methylene-blue dye test and complement-fixation test, usually is sufficient. Organisms can be isolated from body fluids or tissue in some cases. In late infancy and early childhood the sequelae of the congenital infection appear, namely, hydrocephalus, deviations of the eye, and mental retardation.

The methylene-blue dye test and complement-fixation test are of value in helping to diagnose the disease in the first five years of life. After this time, the antibody levels drop and most diagnoses are very presumptive. Relapse of the chorioretinitis does not seem to affect the dye-test titer.

In the normal population the incidence of positive dye tests varies from age group to age group (low in the young and the old, and highest in middle-age groups), in various sections of the country, and in various parts of the world. The general incidence of about 40 percent of positive dye tests in the general adult population in this country makes the diagnosis of toxoplasmosis of the eye extremely difficult. Unless high titers are present (1:1,024 or more), or a fourfold increase or decrease in titer occurs on serial testing, one is not justified in making a presumptive diagnosis. Most uveitis cases have titers of a low level (1:16-1:256), and in such cases one cannot place much value on the serologic result. Since the methylene-blue dye test is expensive to run, and many aspects of its use and interpretation have not been elucidated, it is not *as yet* recommended as a *routine* procedure for the diagnosis of uveitis cases.

The complement-fixation test has little value at the present time in the diagnosis of ocular toxoplasmosis.

Skin-testing antigens are of value only for population surveys, and provide little evidence as to the causation of an individual case of uveitis. Most uveitis cases with positive skin tests have dye-test antibodies in the serum in low titer, but the skin test provides no information as to the level of antibody, therefore it is unsatisfactory for diagnosis. Also, a negative skin test is of no value because a fair percentage of patients have positive dye tests and negative skin tests. Skin testing antigens also require standardization.

The chorioretinitis of ocular toxoplasmosis is not different from that due to other causes, although most lesions are large, produce heavy vitreous opacification, and tend to recur.

The results of testing 644 patients with various types of uveitis indicate that the incidence of positive dye tests is higher (60 percent) in the 0-20 age group than in the 20-50 (30 percent), and 50-70 (20 percent). A correlation was obtained between the severity of the chorioretinitis and the presence of a higher dye-test titer. One patient had a bilateral chorioretinitis and a dye-test titer of 1:30,000 nine months after an acute systemic disease.

Chorioretinitis cases had a much higher incidence of positive dye tests (48 percent) than those with iridocyclitis (23 percent). Among a miscellaneous group of 106 cases were 12 patients with optic neuritis who had low or negative dye tests. All the other cases, which included scleritis and episcleritis, retinal periphlebitis, Eales' disease, and Coats' disease, showed no serologic evidence of toxoplasmosis.

Aqueous humor dye tests were found to be of no value in aiding the diagnosis of ocular toxoplasmosis.

A group of patients having suspected ocular toxoplasmosis were treated with Daraprim (25 mg. three times daily) and sulfadiazine (1.0 gm. four times daily). This treatment, when carried out for three to four weeks, did not seem to affect the inflammatory foci. This result is not surprising, however, when one considers the nature of the parasite, and its intracellular localization.

Discussion. DR. HAROLD G. SCHEIE: Dr. Hogan, of what value is the methylene-blue dye test in mothers? Also, from a practical standpoint, how far should any practitioner go in studying patients for toxoplasmosis?

DR. MICHAEL J. HOGAN: I think the methylene-blue test on mothers is of importance only to help the person who happens to be investigating toxoplasmosis. If the infant's test is positive, the mother's test almost certainly will be positive, but usually not in as high a titer, so it really is not essential to have the mother's dye test.

The reason I selected this discussion for tonight is that I think we should attempt to survey uveitis cases as we have always done employing the means we have at hand. As far as toxoplasmosis is concerned, I think it is very well to perform a skin test providing one keeps his tongue in his cheek, and does not place too much emphasis on the result, except for a negative test. I do not think that one should request laboratories or the public health service to perform routine methylene-blue dye tests on patients with uveitis; the reason for this is that the result of a single test is of no value, and it is impossible at the present time for any laboratory to carry out serial tests on patients with chorioretinitis. Therefore, I would be content with ruling out all other possible causes of uveitis, and if they were negative, and if the patient had findings of what I thought were the possible chorioretinal lesions of toxoplasmosis, I would consider treatment with Daraprim and sulfadiazine, and I would watch the lesions very closely. It is possible to give a smaller amount of Daraprim in a dosage of 25 mg. twice a week plus sulfadiazine two gm. a day over a 15 to 30-day period. This regime might prevent the escape of organisms from cells, their proliferation in the extracellular tissues, and therefore favor gradual healing of the disease. I think that would be the next step as far as our investigations are concerned. I think it would be a lot safer from the standpoint of the patient, too, but at the present time I do not think we should encourage routine testing of sera. Ophthalmologists should not request the routine testing of sera, because the tests are not of sufficient value to help in the diagnosis of the disease. Our experience, as presented here tonight, demonstrates the inadequacies in the diagnosis of this disease.

DR. W. O. LAMOTTE: Dr. Hogan, if you answered this in the substance of your paper, I might have been asleep, but I do not think so. Is there any evidence that the performance of skin tests affects in any way the positivity of subsequently performed methylene-blue dye tests?

DR. MICHAEL J. HOGAN: There is a variation of opinion on this point. Some observers feel that the skin test results in positive dye tests, and others feel the opposite is so. So it is perfectly all right to skin test if you happen to desire a dye test on a patient. If one does a skin test, and then takes serum anytime within the subsequent 48-hour period, the test will not affect the serum antibody level. After the 48-hour period, when the skin test becomes positive, the serum antibody may rise. This point needs further clarification.

DR. IRVING H. LEOPOLD: Have the titers been correlated between the different laboratories, and is there any practical significance of serum neutralization? Is that used at all any longer?

DR. MICHAEL J. HOGAN: The rabbit neutralization test is not done as far as I know any more. We gave it up quite a while ago, because we found that we could produce a positive test depending on which part of the rabbit's back we injected the antigen. There is fairly good correlation between various laboratories, and we have checked our results with several groups. There is not too much difference in the outcome of the results of most of the testing that is done. We have found our results are reproducible on the same sera. Also our results with experimental infections have been satisfactory.

DR. ALLEN: Can the average clinical labo-

ratory do many of these tests?

DR. MICHAEL J. HOGAN: No, the test is rather complicated. It is not an easy test to do, and is fraught with a little danger. We have to handle live organisms, and Toxoplasma is not one which is safe to be careless with. There have been four laboratory technicians which I know of who have definitely acquired acute toxoplasmosis following the handling of organisms. Some deaths occurred.

The test also is fairly expensive, and the average laboratory would not find it practical to run a few tests. Therefore, I think it is a test which cannot be run by the average laboratory. If some of you feel as though you wish to have it done, it might be advisable to get your State Public Health Laboratory to set up tests for your own particular area. Our problem has been that we have been willing to test sera for physicians who send them on suspected cases, but we get a fair number of sera from patients with degenerative diseases. We have been testing sera sent by mail, and have found it impractical so that we do try to discourage the testing of sera except on patients with active and progressive chorioretinitis.

DR. KEENEY: How early in life can calcifications be found in toxoplasmosis, and do calcifications ever occur in adult toxoplasmosis affecting a laboratory worker?

DR. MICHAEL J. HOGAN: The laboratory worker who died definitely had toxoplasmosis with involvement of the viscera, the brain, the lungs, liver, and spleen, and so forth. This disease progressed so rapidly that the patient died before degenerative changes occurred in the brain. The calcifications in children can develop fairly quickly, I would say in one to two months. In some of the children who develop the disease prior to birth the calcifications are already present at birth. In those children who develop the disease one month after birth, a calcification usually can be found at the second to third month. Calcifications are not an important sign of adult acquired toxoplasmosis.

DR. HAYT: Do any special precautions have to be taken in the collection of blood specimens and in their shipment to the laboratories for examination?

DR. MICHAEL J. HOGAN: The whole blood is collected and allowed to clot. The separated serum can be placed in a Wassermann tube and sealed with a flame. It can then be shipped by ordinary or airmail, and does not have to be registered. We ordinarily add a little merthiolate when we ship, but I think if it is handled carefully and put in sterile Wassermann tubes there is very little danger of contamination.

QUESTION: When one is confronted with a case of toxoplasmosis, can a history usually be obtained of any systemic disease compatible with toxoplasmosis which might have been acquired in adult life?

DR. MICHAEL J. HOGAN: Usually not. It has been unfortunate that so far no one has been able to uncover any transmitting agent which is common in all mothers who have given toxoplasmosis to children. A few mothers have been exposed to cats or dogs, and the dogs were said to have sickened and died during the course of pregnancy. We know the disease can exist in dogs, and it is possible that in some way infected household animals or nearby pets may make it possible for the disease to be transmitted to the affected mother. The mother, strangely, never shows evidence of any illness during the course of her pregnancy.

DR. WILLIAM T. HUNT: Has there ever been a toxoplasmosis in a subsequent child?

DR. MICHAEL J. HOGAN: Only one case which I know of. Dr. Arlington Krause, of Chicago, described it to me personally. The mother gave birth to two consecutive children with toxoplasmosis.

William E. Krewson, 3rd,
Clerk.

AMERICAN JOURNAL OF OPHTHALMOLOGY

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EVOLUTION OF CLINICAL PERIMETRY

Just 100 years ago Albrecht von Graefe introduced clinical perimetry (Untersuchung des Gesichtsfeld bei amblyopischen Affectionen, Arch. f. Ophth., **2**(pt. 2) :258-298, 1856). He used but a bit of chalk at the end of a wire and a small blackboard held by the patient at a distance of 18 inches. This simple apparatus, comparable to the Peter hand campimeter, was the basis of a remarkable contribution, as evidenced by the following cuttings from the translation by R. I. Lloyd:

"In determining central visual acuity, we are yet not all informed concerning the patient's faculty of vision. A number of pathological conditions are manifest for a time by the changes in eccentric vision only. Some patients who can read the finest print experience the greatest difficulty in walking abroad

alone. In examining their eyes we find an almost completely intact central vision with a highly restricted eccentric vision. In this respect there is one important disease which I must discuss in detail. We observe in the equatorial areas dark masses of pigment attached to the inner aspect of the choroid, radiating in star-like formation and often appearing like bone corpuscles. This change, which is originally restricted to the equatorial sections, gradually progresses toward the posterior pole of the eye and simultaneously distinct symptoms of optic nerve atrophy present themselves. Judging by its course and the basic changes present, we cannot very well consider it an inflammatory process; the frequently occurring hereditary diathesis would also indicate other trophic changes.

"Particularly instructive for the physiology of the optic nerve are the hemianopic restrictions in cerebral diseases. How can we explain these extraordinary restrictions which occur with such remarkable regularity? Retinal anesthesia beyond a vertical dividing line is observed as distinctly as in anesthesia starting at the median line after severing of the trigeminal nerve. This can only be due to the distribution of the nerve elements, and apparently confirms the recently established theory of a semi-decussation of the optic nerve. The second kind of hemianopia, in which both inner retinal halves are anesthetic, usually presents symptoms indicating some pressure at the base of the cranium. This kind of hemianopia never stops so sharply in the median line as does the other kind."

Von Graefe continually stressed the importance of visual fields in diagnosis. In his article on the glaucomas in 1869 he described in amazing detail the visual field in glaucoma simplex, including the fingerlike defects about the blindspot and the nasal step.

Von Graefe's studies did not extend to the peripheral limits of the visual field or to the use of colors. These investigations were undertaken by Aubert and his co-worker, Foerster—a by-product being Foerster's arc perimeter, introduced in 1869. After the advent of this perimeter, von Graefe's method of campimetry (a designation coined by J. Hirschberg in 1875) fell into gradual desuetude until revived by Bjerrum in 1889. Among the early modifications of the perimeter were Stilling's ground-glass globe (1877), a self-registering device exhibited by Stevens of New York (1881), and the Schweigger hand perimeter (1889).

To Bjerrum is due the conception of quantitative perimetry. He noted the isopters of small white objects of different sizes at a distance of one to two meters from his black-velvet screen. Lloyd comments:

"The mad rush from the perimeter to the campimeter which followed the publication of his article was much like the earlier stampede from the campimeter to the perimeter."

Quantitative perimetry adds to the informative data. To the neurosurgeon a defect with a sloping edge suggests hope for some recovery. In glaucoma, a defect with a steep slope indicates neural involvement while a gradual slope suggests a circulatory disturbance. In some cases, only more delicate methods reveal a reduction in sensitivity. The simplest is to expose two targets simultaneously on opposite sides of the fixation point and at equal distances from it. The inability to see the target in the affected field is dependent, according to Bender (1952), on gradients of excitability; according to I. M. Allen (1948) on visual attention. The phenomenon is observed in disturbances of the brain but not of the optic nerve. Bay more recently used the same method to test local adaptometry; the fading time is decreased in the affected area. Flicker fields are often superior to standard perimetry in detecting regions of minimal depression, including the central area in retrobulbar neuritis. For the study of flicker fields in the office the Strobotac device is now available.

Colored test objects have a restricted use; the peripheral limits of a color field are

difficult to define as the discrimination between hue and luminosity is too often uncertain. When the media are cloudy, however, the field for color may be more reliable than that for white as color perimetry is less influenced by blurred images. Colored test objects are most useful in the central fields; the presence of a three- or five-mm. red object is easier to determine than that of a one-mm. white object. In 1953 Harrington introduced test objects of sulfide inks rendered luminiscent by ultraviolet. These colors are essentially monochromatic and of greater purity and saturation than those previously available. This innovation should give color perimetry a new impetus.

Haitz utilized the Holmes stereoscope to maintain steady fixation, using paired charts in which the fixing point on one was marked by a colored dot. To overcome the limitations of this simple apparatus in which the usable area was limited to 11 degrees from the fixation point, Lloyd developed the stereocampimeter. Evans, using his own modification of this device, showed that the earliest field defect in glaucoma simplex is a widening of the angioscotomas. Recently Hobbs of London has adapted the stereoscopic principle to the Bjerrum screen by having the fellow eye focus at a replica target in the synoptophore.

The obstrusive wand is no longer required —the magnet has been substituted in the magnetic campimeters (Spaeth, 1954; Gunkel and Ryan, 1955), and the Raiford dome perimeter (1954); and the projected light spot in the various projection perimeters and campimeters. The latter instruments are ideally adapted to quantitative perimetry, permitting a rapid diminution in the size and contrast of the test object and of the general illumination.

Cushing was probably the first neurosurgeon to insist upon routine quantitative perimetry in the investigation of cerebral lesions and demonstrated the diagnostic value of repeated and thorough study of the field of vision. Unfortunately, many candidates for certification by the American Board of Ophthalmology have not been similarly impressed. Cordes, in an editorial, "Plea for better instruction in perimetry" (THE JOURNAL, **29**:745, [June] 1946) remarks:

"If the field is to be of any value it must not only be properly taken, it must also be properly interpreted. . . . In too many institutions the taking of the fields is left to a technician."

Vail, in a later editorial, "Perimetry," (THE JOURNAL, **30**:1182, [Sept.] 1947) notes:

"It is the duty of every department of ophthalmology to conduct a stimulating and satisfactory course in perimetry. . . . The taking of a visual field remains, and always will remain, an art."

Any difficulty in seeing that cannot be otherwise explained calls for a visual field study. The tachistoscopic device of Harrington and Flocks (1955) provides a simple satisfactory screening test that can be performed in a few seconds. It consists of a series of simple abstract patterns printed in white fluorescent sulfide ink which become momentarily evident by a flash of ultraviolet. This rapid test could well be included in the visual examination of motor vehicle drivers.

From von Graefe to Traquair the giants of ophthalmology have contributed bit by bit to the art and science of perimetry. As Anav, a 13th century Hebrew scholar, said, thanks to this heritage: "Like pigmies riding on giants' shoulders, we see farther than the giants, when we use their knowledge and experience."

James E. Lebensohn.

INTERNATIONAL COUNCIL OF OPHTHALMOLOGY

The following is a résumé of the minutes of the annual meeting held in Paris on May 5, 1956:

Present were: Duke-Elder (president), Berens (vice-president), Hartmann (secretary), Amsler (treasurer), Bietti (president, International Organization against Tra-

choma), Coppez (president, International Congress, Brussels), Franceschetti (president, International Association for the Prevention of Blindness), Payne (president, Pan-American Association of Ophthalmology), Alvaro (Brazil), Arruga (Spain), Charamis (Greece), Lyle (Great Britain), Marshall (Canada), Paufique (France), Thiel (Germany), and Weve (Holland). Present by invitation were: François (secretary, International Congress, Brussels) and Copper (editor, *Index Ophthalmologicus*).

Routine reports were made by the president and the treasurer dealing with the general position and the affairs of the council during the previous year.

International Dictionary of Ophthalmological Terms. It was reported that the authors of the various languages (Alvaro, Arruga [Spanish], Amsler [French, German], Bietti [Italian, Latin] and Duke-Elder [English]) had completed their work and that the manuscript of the dictionary was now in the hands of the printers.

Index Ophthalmologicus. Arrangements were made for the publication of the *Index Ophthalmologicus* (the world directory of ophthalmologists, ophthalmic hospitals, and so forth) at the International Congress in Brussels in 1958.

XVIII International Congress in Brussels in September, 1958. It was decided that the administrative languages would be English, French, and German, and that the ordinary subscription would be 1,500 Belgian francs with an addition of approximately 10 percent for those attending who are not members of a society affiliated with the federation, and a reduction to approximately 30 percent for associates or scientific associates. If the Acta of the Congress were to retain its previous luxurious form, the subscription to the congress would have had to be increased; permission was therefore given to the Belgian Organizing Committee to reduce their commitments in printing the Acta so that their expenses would be covered by this subscription. The main discussions were chosen as: "The orthoptic (nonoperative) treatment of strabismus," and "Gerontology in ophthalmology." For the first, the following were to be invited as opening speakers: Lyle, Malbran, and Bangerter; for the second: François, Buerger, and Jayle.

European Ophthalmological Society. The creation of a European Ophthalmological Society on lines similar to those of the Pan-American Association of Ophthalmology was discussed and it was decided that François (Belgium) and Riise (Norway) would explore the possibilities of creating such a society and report to the council at the next meeting.

The organization of international congresses. A considerable discussion took place on changes which might be introduced in the organization of future international congresses, and a subcommittee consisting of Alvaro, Berens, Duke-Elder, and Thiel was appointed to present a report to the next meeting of the council.

Committees on road safety. The committee charged with studying optical problems associated with safety on roads presented an interim report, and an interim report was received from Blum (Geneva) acquainting the council with the work of the consultant group on medical requirements in the licensing of motor vehicle drivers.

Statutes and rules. A discussion took place on the statutes of the International Federation, the International Council, and the internal organization of international congresses; the president and secretary were asked to prepare a report before these statutes were finally confirmed at the International Congress in 1958.

History of International Ophthalmological Congresses. In view of the fact that the Congress in Brussels nearly marks the centenary of the I International Congress, it was suggested that the president prepare a short history of these meetings during the last hundred years.

The next meeting of the council will be held in London on April 10, 1957.

CORRESPONDENCE

More on orthography

Editor,

American Journal of Ophthalmology:

Further anent distichiasis, districhiasis, and so forth.

After the October and December (1955) issues I wrote you a comment but did not mail it as it was almost, if not entirely, pure pedantry. But since Dr. Burian has been so bold I will go ahead with my bit.

Dr. Fox is, of course, to be congratulated in decrying the misuse of districhiasis for distichiasis and in even being horrified at dystrichiasis. Contrary to Dr. Fox's statement, though, there is such a word as districhiasis, and the fact that there is such a word helps to point up the deeper reasons for there being such misuses and mistakes, and, worse still, the existence of words with no meaning at all. It is my contention that it is not so much our lack of at least some familiarity with the Greek and Latin roots, but rather the liberties taken in the original coinage of certain of these medical words or the adulterations that have taken place since.

Districhiasis is the word for two hairs growing from one follicle (Dorland). I happened to stumble onto it a few years ago while looking up distrix. But even if no such word were in the dictionary we could easily make one since a single wood for two hairs has as much justification as a single word for two rows. Distrix, incidentally, is defined as the splitting of hairs at their distal ends. Since districhiasis and distrix are obviously the same word the assigning of the meaning of at least one of them was indeed arbitrary on someone's part. But, back to my theme.

It is the not knowing where a prefix ends and the root begins that causes most of the trouble. This can be hidden by the spelling of the word, or, once correctly spelled, by the pronunciation. A few examples will illustrate my point. In my opinion, distichiasis (two rows) should be written and pronounced dis-stichiasis, or better, di-stichiasis; districhiasis (two hairs) should be districhiasis. (Perhaps the intended prefix in distrix, as above defined, was really not dis (Greek) for *double* but dis (Latin) for apart, as in dissect.) The absurd word hyphemia should be hypo-hemia to have any meaning whatever, and extravasation should be extra-vasation. Buphthalmos should be thrown out altogether since it would still be a horrible word even written correctly, bous-ophthalmos. On a less lofty plane, I can see no reason why the front part of the head cannot be fore-head (rather than the insipid fored), and it is a delight to hear an Englishman or a Blue Ridge mountaineer (still Elizabethan) unashamedly so pronounce it.

But enough windmills for today and, besides, any linguist can no doubt show that the words are correct as they are. In the meantime, for those not already familiar with it, let me commend to them the delightful little volume of the late Dr. O. H. Perry Pepper, *Medical Etymology* (W. B. Saunders, 1949).

(Signed) Harry M. McAllister,
Atlanta, Georgia.

BOOK REVIEWS

Strabismus. By Beulah Cushman, M.D. Philadelphia, Lea & Febiger, 1956. Price: $6.00.

This small volume comprising less than 150 pages of text is concerned essentially with re-emphasizing the doctrine of Alexander Duane and James W. White. The book is dedicated to the latter author, and Dr. Cushman has shown that she is an ardent and faithful disciple.

Unlike many of the textbooks on this subject that have appeared in the past two decades, this book presents no theories and is devoted almost entirely to the objective measurement of the angle of squint and the surgical correction thereof.

The author believes that horizontal and

vertical muscle abnormalities are on a basis of anomalies of innervation, insertion, or structural changes in the muscle itself. She believes that innervational abnormalities constitute the largest number of muscle problems and states that 90 percent of squints have a vertical anomaly. She further feels that the superior rectus muscle is involved much more frequently than the superior oblique.

Though the author says that innervational factors are the most important cause of strabismus, she seems to favor an anatomic surgical approach; that is, recessions or advancements measured to the 0.5 mm. Her surgical judgment is excellent, and there is no question that many failures are due to poor preoperative diagnosis and the resultant improper surgery. The reviewer, however, feels that, in many instances, if the eyes are placed approximately in a parallel position, something takes over and the patient develops binocular vision, fusion, and so forth. There are another group of patients frequently with five to 15 degrees of esotropia in which a functional result is rare despite two or three surgical procedures.

This book is written for postgraduate students and ophthalmologists, and should be read by all who attempt any type of muscle surgery. There are too many ophthalmologists who rely solely on the measurements of their orthoptists, or who, in a brief examination of the ocular excursions, decide which muscle or muscles should be operated on. There are not many who will be able to perform the objective measurements or interpret the results as well as Dr. Cushman does but a careful perusal of her monograph will certainly be of great value to the reader. I am sure that Dr. James W. White would be proud of Dr. Cushman's presentation.

P. Robb McDonald.

SURGERY OF THE EYE: DISEASES. By Alston Callahan, B.A., M.S. (ophth.), M.D. Springfield, Illinois, Charles C Thomas, 1956. 425 pages, 263 illustrations, 19 color plates, references, index. Price: $25.00.

This is the companion volume to *Surgery of the Eye: Injuries*, published by Thomas in 1950. It shows the same high quality of paper, printing, and illustrations. The two volumes cover the field of ophthalmic surgery in a most excellent fashion and our libaries in this field are made the richer by the present contribution.

The author had much surgical experience during the war and since, and is obviously a deep student and an expert operator. The book reflects, therefore, not only extensive reading and an insatiable curiosity, but, which is more important, ingenious applications of surgical facts and sound clinical judgment based on his own wide experiences. He has clung to that which he considers good, discarding those procedures that he has found to be unsound, and has come up with a textbook on eye surgery that is indeed most modern.

The chapters include anesthesia, congenital anomalies of the lid, blepharoptosis (good), entropion and ectropion, surgery of lid tumors, lids, lacrimal apparatus, congenital anomalies and diseases of the eye, conjunctiva and cornea, iris, cataract (particularly good chapters that cover the subject from preoperative care to late complications and so forth), six good chapters on glaucoma surgery, surgery of the sclera, retina and vitreous, two excellent chapters on the extraocular muscles, removal of the eye and implants, a fine chapter on the surgery of the orbit, and two chapters on advances in the management of injuries of the eye and adnexa.

The text is clearly written and the excellent illustrations are most pertinent to the subject that is being discussed, so that the reader can follow each step in meticulous detail. This in itself is evidence of the clear thinking and sound judgment of the author. It is a profitable pleasure to read and refer to Dr. Callahan's book. All eye surgeons, re-

gardless of the number of years of their experience, will find it most useful.

Derrick Vail.

PUBLICATIONS: AMERICAN FOUNDATION FOR THE BLIND, New York, 1956

FILMS RELATING TO BLINDNESS AND WORK WITH BLIND PERSONS. Edited by M. R. Barnett. 20 pages. Price: 35 cents.

This catalog lists the numerous films now available on the many aspects of blindness. Most of the entries are 16-mm. motion pictures with sound; some are in color. The running time ranges from 10 to 60 minutes.

PERIODICALS OF SPECIAL INTEREST TO BLIND PERSONS. Edited by M. R. Barnett. 35 pages, index. Price: 35 cents.

Four braille periodicals are published in Canada and 102 in the United States. Eight are reprints of inkprint current events papers. Nine periodicals are published as Talking Books.

ASSOCIATION FOR THE PREVENTION OF BLINDNESS, BENGAL. Silver Jubilee Bulletin. Calcutta, Sri Gouranga Press, 1955. 74 pages with illustrations. Price: Rs 0.12.

The Association for the Prevention of Blindness in Bengal is a private organization, though generously subsidized by public and civic funds. The project was inspired by the late Mrs. Winifred Mather, founder of the New York Association for the Blind, who visited Calcutta in 1929 and donated the initial contribution and two educational films. Propaganda has extended to lectures, posters, radio talks in English and Bengali, census studies, and prize contests on the theme of blindness prevention. The rate of blindness (inability to count fingers) is very high, 14 per 1,000—sevenfold that in the United States. An extensive study has shown that 50 percent of the blindness was curable, and another 42 percent preventable. Among the major causes of blindness are smallpox, keratomalacia, epidemic dropsy glaucoma, couching for cataract, and trachoma. Since 1949, the West Bengal government has opened dispensaries and hospitals throughout the country. The association itself sponsors five travelling eye dispensaries, one for each division of Bengal. The criteria for the various degrees of blindness are discussed by various authorities. Dr. Franklin M. Foote notes that, from the standpoint of the United States federal income tax, blindness is defined as a corrected acuity of 20/200 or less in the better eye or a visual field reduced to 20 degrees or less in its widest diameter.

James E. Lebensohn.

HISTORIA DE LA OFTALMOLOGIA EN VENEZUELA HASTA 1955. By Jose Manuel Espino. Caracas. Imprenta Nacional, 1955. Paper-bound, 242 pages. Price Not listed.

This extensive and detailed history of ophthalmology in Venezuela is conveniently provided with adequate three-page summaries in Spanish, French, German, and English. The first of nine chapters is devoted to a description of native therapeutics, the second to the colonial era before ophthalmologists were available. The modern period begins with the opening of the Vargas Hospital in Caracas in 1891. The work and publication of the outstanding ophthalmologist is recorded in detail. Further chapters deal with ophthalmology and public health, the teaching of ophthalmology, the ophthalmological societies, a directory of all Venezuelan ophthalmologists and their bibliographies, and the status of optometry in Venezuela. All the information that one could desire is perspicuously arranged from several points of view and the book is a mine of complete, easily accessible information.

F. H. Haessler.

ABSTRACT DEPARTMENT

EDITED BY DR. F. HERBERT HAESSLER

Abstracts are classified under the divisions listed below. It must be remembered that any given paper may belong to several divisions of ophthalmology, although here it is mentioned only in one. Not all of the headings will necessarily be found in any one issue of the Journal.

CLASSIFICATION

1. Anatomy, embryology, and comparative ophthalmology
2. General pathology, bacteriology, immunology
3. Vegetative physiology, biochemistry, pharmacology, toxicology
4. Physiologic optics, refraction, color vision
5. Diagnosis and therapy
6. Ocular-motility
7. Conjunctiva, cornea, sclera
8. Uvea, sympathetic disease, aqueous
9. Glaucoma and ocular tension
10. Crystalline lens
11. Retina and vitreous
12. Optic nerve and chiasm
13. Neuro-ophthalmology
14. Eyeball, orbit, sinuses
15. Eyelids, lacrimal apparatus
16. Tumors
17. Injuries
18. Systemic disease and parasites
19. Congenital deformities, heredity
20. Hygiene, sociology, education, and history

3

VEGETATIVE PHYSIOLOGY, BIOCHEMISTRY, PHARMACOLOGY, TOXICOLOGY

Matsusaka, Tochikiko. **Histochemical study of the retina. Effect of iodoacetic acid on glycogen and nucleic acid in the inner segment of the visual cells of the retina.** Ann. d'ocul. **188**:1071-1075, Dec., 1955.

Intraperitoneal injections of iodoacetic acid in fowl caused a decrease and then a disappearance of the pink coloration of glycogen granules in the visual cells of retinas stained by Hotchkiss-McManus. No effect on nucleic acid was noted, using Feulgen's method, but with Brachet's technique, there was a decrease in visible pyronines. (5 figures) John C. Locke.

Owe-Larson, A. **The local effect of noradrenaline on the eye.** Acta Ophth. **34**:27-34, 1956.

The literature on noradrenaline and its effect on the eye are reviewed in detail and the author's own investigations are reported. These concerned the effect on the pupil of a two and three percent noradrenaline solution instilled into the conjunctival sac. The data show that preliminary instillation of tetracaine or tonometry was necessary before mydriasis could be induced by the noradrenaline solutions. The author's data do not confirm Hoffman's report that noradrenaline by itself dilates the pupil. There is the possibility that his solution contained some other physicochemical agent which facilitated the penetration of this drug through the cornea. Preliminary instillation of pontocaine or tonometry was followed by noradrenaline mydriasis which showed considerable individual variations in its size. The maximum dilation occured in less than an hour, and was of short duration; the pupil may be eccentric in the early part of dilatation, with the greatest dilatation nasally and downward. The effect of pontocaine and tonometry is attributed to a traumatization of the corneal epithelium, which facilitated the penetration of the noradrenaline through the cornea; it is not believed that it is due to a process of sensitization of the cornea by the local anesthetic. In addition to mydriasis noradrenaline produced regularly a very strong local anemia and a moderate cycloplegia. Occasionally there was a reduction of ocular ten-

sion. In cases of secondary glaucoma noradrenaline was found to lower the ocular tension in the same way as other adrenaline preparations. (1 figure, 1 table, 12 references) Ray K. Daily.

4

PHYSIOLOGIC OPTICS, REFRACTION, COLOR VISION

Capalbi, S. and Andreani, D. **A study of heredity of anisometropia.** Ann. di. ottal. e clin. ocul. **81**:512-516, Nov., 1955.

Statistical methods were applied to the findings in 39 families in which anisometropia occurred. The condition is shown to have recessive characteristics, and to be independent of the presence of ametropia. (1 figure, 1 table, 7 references) John J. Stern.

Mahneke, Axel. **Flicker fusion thresholds.** Acta Ophth. **34**:112-120, 1956.

The main objective of this study was to determine what experimental conditions account for the fact that the time of the appearance of the flicker by lowering the frequency, and that of the disappearance of the flicker by increasing the frequency do not coincide. Three subjects were used and the experiments are described in detail. The transition of the flicker into a continuous light is taken as the threshold of flicker fusion, and the recognition of the flicker from a continuous light is termed the flicker discrimination. The data show that these two responses are influenced differently by changes in acceleration of frequency, but they do not afford a final explanation for the difference demonstrated between the two thresholds. (1 figure, 1 table, 13 references) Ray K. Daily.

Rönne, Gerhard. **The physiological basis of sensory fusion.** Acta Ophth. **34**:1-26, 1956.

The literature is reviewed and the author's investigations are reported. The detailed report of the laboratory experiments on the binocular perception of identical stimuli and on the mechanism of integration of disparate stimuli supports the conclusion that binocular perception is based on integrative processes which are initiated by the stimuli reaching the two retinas; the integration takes place in the occipital cortex, and is based on an anatomophysiological substratum comparable to an electronic gear.

The surface of reference of the subjective visual space, or horizon, is determined by an innate correspondence of pairs of ganglion cells in the visual center; coupling of others than these cells results in depth perception in relation to the surface of reference. The condition for coupling is the identity of the stimulus in the two layers of the ganglion cells, or a disparity below a certain limit. If the limit of disparity is passed a motor impulse tends to diminish the disparity, thereby changing the surface of reference or the horizon. A number of unphysiologic stimuli may destroy the normally existing isomorphism between objective and subjective space, but the resulting perception, nevertheless, follows a certain scheme of action. The integration of a disparity pattern necessitates inhibition of corresponding elements which receive unidentical stimuli. Integration of disparate but identical stimuli and inhibition of nondisparate unidentical stimuli are complementary expressions of the same basic mechanism. Identical stimuli reaching corresponding retinal cells are integrated and visualized with reference to the horizon. Unidentical stimuli reaching corresponding cells cannot be integrated; one of the stimuli is inhibited and does not reach perceptual level. Cortical integration can be increased or diminished by repetition or training, and on this fact rest the procedures of orthoptic treatment. Stereopsis, integration of disparate impulses, and retinal rivalry are linked closely together, and observations of the

simultaneous cessation of retinal rivalry and disappearance of sensory fusion and stereopsis during intoxication demonstrate that integration and suppression are virtually complementary expressions of the same basic process. Experiments on the synoptophore showed a close parallelism between the decrease in disparity limit and increase in heterophoria. Retinal rivalry experiments definitely demonstrate the presence of inhibition, the intensity of which may be varied by different means. In the extremely intoxicated individual, and in subjects with horror fusionis, inhibition is completely absent, and the two uniocular stimulus patterns are present in consciousness independently. (15 figures, 16 references)
Ray K. Daily.

Ryan, Vernon. **A critical study of visual screening.** Am. J. Optometry **33**:227-257, May, 1956.

After a review of the literature, the author concluded that visual screening in the schools should be kept simple, and should be done by a technician instead of a professional. "When properly administered, the Snellen test at distance is undoubtedly the best single test available for vision screening." In addition, tests should be made for hyperopia and muscle balance. Paul W. Miles.

Salgado, E. **Treatment of degenerative axial myopia by scleral resection.** Ann. d'ocul. **189**:217-226, Feb., 1956.

In 25 cases of degenerative axial myopia treatment by lamellar scleral resection is reported. The operation consists of removal of a strip of sclera, two to four mm. in width and two-thirds of its thickness deep, from one half of the circumference of the globe. The procedure is well tolerated and seems to check future progress of the disease. It has a favorable effect on choroidal circulation, protects against further distension of the sclera, and against retinal detachment and hemorrhages of myopic origin. A reduction in the myopia of 6 to 8 diopters usually results. Either an increase or decrease in astigmatism may occur, depending upon its axis. John C. Locke.

5

DIAGNOSIS AND THERAPY

Berezinkskaya, D. **The role of ophthalmodynamometry in the diagnosis of changes in the fundus.** Vestnik oftal. **1**:17-18, Jan.-Feb., 1956.

Ophthalmodynamometry was performed on 81 patients in the Moscow Central Institute; of these 35 had chorioretinitis of various etiology; 6 had a neoplasm of the choroid, and 40 a diseased optic nerve. The blood pressure and ocular tension were normal in all patients.

Inflammatory processes in the optic disc and in the choroid near the disc usually are accompanied by a decrease of the pressure in the central artery.

In noninflammatory chorioretinal changes there is no decrease of the diastolic pressure. An increase of the pressure was found in neuropathy of the optic disc but none in optic neuritis. Ophthalmodynamometry is recommended as one of the methods of diagnosis of intraocular neoplasm. Olga Sitchevska.

Browning, Carroll W. **Evaluation of beta irradiation therapy in ophthalmology.** South. M. J. **49**:298-303, March, 1956.

Beta radiation is not the treatment of choice in neoplastic lesions of the lid and skin; it is useful for small flat lesions of the globe. Beta radiation may be used soon after surgery for the removal of pterygium to prevent the regrowth of vessels and tissues. It may also be used in vernal catarrh when hydrocortisone has failed to relieve the patient's symptoms. Treatment should never be given more often than every three weeks unless a cumulative effect is desired. Each pa-

tient receiving beta therapy should have the peripheral portion of his lens examined every six months for six years. A focal beta-radiation cataract has been observed and it is not known that the opacity will be permanently limited to the size of the treatment sector and will not decrease visual acuity or impair peripheral vision. Whether the focal beta-radiation cataract can potentiate or enhance the development of senile cataract is also unknown. (18 references)

Irwin E. Gaynon.

Dubilier, W., Jr., Von Gal, H., Freemond, A. and Evans, J. A. **Orbital pneumotography.** Radiology **66**:387-392, March, 1956.

Tomograms are taken at various levels of the orbit after the injection of 15 cc. of air into the muscle cone and 2 cc. of air above the muscle cone. It is of greatest value in unilateral exophthalmus in which an orbital tumor is suspected. This procedure is not only useful in establishing the presence of a tumor, but also in localizing it. (8 figures, 1 reference)

Irwin E. Gaynon.

Junghannss, Karlheinz. **The suction cup in ophthalmology.** Klin. Monatsbl. f. Augenh. **128**:332-336, 1956.

More than 20 years ago Herzau constructed a glass cup which can be put on the cornea and conjunctiva. The cup is connected with a rubber balloon and in this way suction can be exerted for 5 to 10 minutes. This causes a passive hyperemia which may be of benefit in corneal inflammations and scars as well as in acute occlusions of retinal blood vessels. (3 figures, 13 references)

Frederick C. Blodi.

Kennedy, Patrick J. **Treatment of cysts of the iris with electrolysis.** A.M.A. Arch. Ophth. **55**:522-525, April, 1956.

The author reports treatment by electrolysis for iris cysts following cataract extraction in six cases. The technique is described and consists essentially in introducing an electrolysis needle into the cyst through a corneal knife-needle incision; 10 to 15 ma. of current are used. (4 references)

George S. Tyner.

Levasseur, J. C., and Porot, J. **A procedure for radiologic exploration of the bony nasolacrimal duct.** Ann. d'ocul. **189**:303-310, March, 1956.

The authors describe a method of tomography (sectional roentgenography) of the bony nasolacrimal duct which gives better results than current standard methods of X-ray examination. (5 figures, 9 references)

John C. Locke.

Offret, G., Saroux, H. and Bisson, J. **Results of studies of the human aqueous during the last two years.** Bull. et mém. Soc. franç. d'opht. **68**:51-57, May, 1955.

About 150 samples of aqueous were examined, using a technique which is slightly different from that of Amsler and Verrey. Bouillon-serum was used instead of blood-agar, albumen was evaluated by the method of Magitot-Mestrazat and the speed of centrifugation in bacteriological examination was increased. Chemical and cytological analyses were performed, the dissociation of the albumen content from the number of cells was investigated and the importance of the presence of organisms in certain types of iridocyclitis was studied. Organisms were found frequently in the uveitis of focal infections and heterochromia.

Alice R. Deutsch.

Pannarale, Mario R. **Experimental and clinical investigations on the use of N. N'dibenzylethylendiamine dipenicillin G (Wycillin A. P. Erba, benzathine penicillin G) in septic affections of the eyeball.** Ann. di ottal. e clin. ocul. **81**:517-533, Nov., 1955.

Among the delayed-action penicillins today in use, N. N' dibenzylethylendiamine dipenicillin G affords the slowest and most gradual absorption. It also has ex-

ceptional stability and local anesthetic power. Subconjunctival injections of D B E D resulted in therapeutically active intraocular concentrations after 12 to 14 days. In experimental septic processes (keratitis and endophthalmia), a single dose of 150,000 units given subconjunctivally displayed a strong action against the pyogenic cocci. In 19 cases of septic corneal ulcers a single injection of 150,000 to 300,000 units under the bulbar conjunctiva near the fornix resulted in speedy recovery with hardly any corneal opacity. In two cases of septic endophthalmia, systemic antibiotic therapy was added to the local injections; in both the eyes were retained, in one case with good functions. (2 figures, 3 tables, 17 references) John J. Stern.

Pires Amarante, Olavo. **The problem of the artificial eye.** Arq. brasil. de oftal. **18**:69-75, 1955.

The social importance of a cosmetically attractive artificial eye is not as well recognized by ophthalmologists as it might be. The loss of the eye coupled with the cosmetic defect of an ill-fitting prosthesis, or no prosthesis at all may result in a marked personality change. Adequate surgical treatment of the socket and delayed implant when indicated are valuable in the rehabilitation of the patient from both an ocular and social standpoint.

A good prosthesis is one which is well adapted to the socket, has movement synchronous with the fellow eye, has a lifelike appearance and does not produce secretion or irritation. An implant is recommended, which may be of any suitable variety. The results in immediate implantation are good, while the delayed implant may not be quite so gratifying. Enucleation with insertion of an implant is generally preferable to evisceration. The choice of implant, sutures, and technique vary according to the wishes of the individual operator. In treating an old socket, contracted, with no prosthesis, the author recommends dilatation with a series of progressively larger prostheses. Plastic reconstruction of the fundus of the conjunctival sac may be necessary if the prosthesis can not be retained.

The prosthesis may be inserted soon after enucleation or evisceration (usually 30 days) in an effort to rehabilitate the patient as soon as possible, even in patients as young as 6 months of age. A properly fitted prosthesis causes no symptoms of irritation, pressure or profuse discharge. Removal at bed time and irrigation of the socket with normal saline are the essentials of ocular hygiene. The use of collyria is discouraged, as further irritation may increase secretion.

James W. Brennan.

Thomas, C. I., Krohmer, J. S., MacIntyre, W. J. and Bovington, M. **Small end-window and angle-window Geiger counters.** A.M.A. Arch. Ophth. **55**:519-521, April, 1956.

An improved instrument is introduced for use in measuring uptake of radioactive ions in eyes after the intravenous injection of radioactive phosphorous. (2 figures, 1 table, 4 references)

George S. Tyner.

Tomashevskaya, A. **The application of cadaver's cartilage in plastic operations in ophthalmology.** Vestnik oftal. **2**:18-22, March-April, 1956.

The eye department of the Sverdlovsk Institute of traumatic and reconstructive surgery used cadaver's cartilage preserved in alcohol for reconstruction of deformed orbits since 1947. The rib cartilage is taken from the cadaver within 24 hours after death; the cartilage is preserved in 70 percent alcohol which is changed daily at first, then once a month. Prior to the plastic operation the cartilage is placed in a warm physiologic salt solution for five to ten minutes, which makes it more elastic and easy to mold to the

required shape. Since the cartilage is not absorbed and becomes incapsulated in the tissues, the results were good.

Since 1947 to 1953, this type of chondro-plastic operation was done on 60 patients, aged from six to 52 years. In 49 patients the deformity of the orbit was the result of gunshot wounds, in seven a result of industrial trauma and in four the sequel of disease of the eye. In 25 patients there was a defect of the lower margin of the orbit, in four of the upper, and in some, lagophthalmos; in 12 patients the cartilage was used for the formation of a stump after enucleation. The technique of the operation and some case histories are described briefly. The cosmetic results were good in most of the patients. Olga Sitchevska.

Verrey, F. **Practical aspects of anterior chamber puncture, and a simplified examination of the aqueous.** Bull. et mém. Soc. franç. d'opht. **68**:40-45, May, 1955.

A short summary on the usefulness of anterior chamber puncture in clinical ophthalmology is given. After describing his technique and suggesting appropriate laboratory procedures Verrey reviews a group of eye diseases for which an investigation of the aqueous proved to be significant. The contra-indications of anterior chamber puncture are hemorrhagic narrow-angle glaucoma and the glaucoma secondary to the heterochromia of Fuchs.
Alice R. Deutsch.

6
OCULAR MOTILITY

Casellato, Luciano. **Classification of the syndromes of disturbances of ocular motility based on the duration of the deviation and the status of the binocular vision.** Ann. di. ottal. e clin. ocul. **81**:507-511, Nov., 1955.

Discussion of The Classifications by Cords (1930) by the authors of Traité d' Ophthalmologie (1939), by Duke-Elder (1949) and by Scobee (1947-52) are discussed and a new classification is proposed with four main categories: 1. Paralyses and Spasms, 2. Heterophorias, 3. Strabismus, and 4. Nystagmus. (5 references) John J. Stern.

Chinaglia, V. and Amidei, B. **Results of occlusion in amblyopia of strabismus.** Ann. di. ottal. e clin. ocul. **81**:563-575, Dec., 1955.

Occlusion, if correctly applied and accompanied by appropriate exercises, can give equally good results as pleioptics. (1 figure, 3 tables, 22 references)
John J. Stern.

Crone, R. A. and Velzeboer, C. M. J. **Statistics on strabismus in the Amsterdam youth.** A.M.A. Arch. Ophth. **55**:455-470, April, 1956.

The authors try to answer, in part, the questions "how many cases come under consideration for orthoptic treatment, which cases, and with what chance for success." These questions were approached by a clinical study concerning the relative frequency of different types of squint as defined by the clinical features. The answers to these questions were not found in these studies. The authors do, however, reach some conclusions regarding the etiology of comitant squint. They state unequivocally that all types and characteristic patterns of convergent squint are hereditary to a practically equal extent. Such factors as hypermetropia and disease are considered trigger factors rather than etiologic ones. (18 tables, 35 references)
George S. Tyner.

Cucco, Giovanni. **The eye movements during reading (investigations by means of photographic registration on moving film with the Master Ophthalmograph).** Ann. di. ottal. e clin. occul. **81**:494-506, Nov., 1955.

The results of the author's investigations of the eye movements during reading are stated to correspond closely to those obtained by American authors. The "fixation pause" occupies 90 percent of the total reading time. The other eye movements, although voluntary, have the characteristics of reflex movements and as such cannot be regulated as to frequency or speed. (3 figures, 1 table, 42 references) John J. Stern.

Folk, Eugene R. **Surgical results in intermittent exotropia.** A.M.A. Arch. Ophth. **55**:484-487, April, 1956.

The author concludes from 50 cases that surgery is the treatment of choice for intermittent exotropia. When the deviation is greater than 25Δ for distance or near, a bilateral 7 to 8 mm. recession of the lateral rectus muscles is indicated. In squints of less degree one lateral rectus muscle may be recessed. (5 tables, 9 references) George S. Tyner.

Hugonnier, R. **The present status of orthoptics—its possibilities—its limitations. Additional observations.** Ann. d'ocul. **189**:311-318, March, 1956.

The more deeply rooted forms of abnormal retinal correspondence can be elicited both on the synoptophore and by Bielschowsky's after-image test, and in these cases orthoptic treatment is not advised. Less severe forms, however, may show abnormal retinal correspondence on the synoptophore (with a scotoma at the subjective angle), but normal positive after-images (the negative after-images may be abnormal). This is because the after-image test is less physiological than the synoptophore, and the more deeply-rooted the A.R.C., the more easily it can be elicited by less physiological means. Orthoptic treatment is indicated in these cases if social and economic conditions are favorable. It is abandoned if no progress is observed after six sessions. A maximum of 30 sessions is usually sufficient, and for socio-economic reasons should rarely be exceeded.

John C. Locke.

Urist, Martin J. **Esotropia with bilateral depression in adduction.** A.M.A. Arch. Ophth. **55**:509-515, April, 1956.

Urist reports 124 cases of esotropia in which the esotropia was greater on supraversion than on intraversion. The majority of patients showed a hypertropia of the abducted eye in looking down and to the right or down and to the left. Glasses which corrected accompanying hyperopia tended to correct the squint for distance more than that for near. (10 tables, 9 references)

George S. Tyner.

7

CONJUNCTIVA, CORNEA, SCLERA

de Gaspare, P. F. Ferraris. **Neomycin with gramicidin in the prevention and therapy of acute seasonal conjunctivitis. Collateral effect on trachoma.** Ann. di ottal. e clin. ocul. **81**:535-544, Dec., 1955.

Fifty persons were given a neomycin and gramicidin ointment twice daily during the season of acute conjunctivitis in Saudi Arabia. No case of conjunctivitis was observed among them, while 27 percent of the untreated controls contracted the disease. In 30 patients with acute conjunctivitis, the application of the ointment four times daily resulted in complete cure in four to ten days. Even in recurrences the ointment retained its effectiveness. The therapy had no effect on trachoma except for the elimination of secondary infections. (No bacteriologic studies are reported.) (2 tables, 18 references) John J. Stern.

Kurz, M. **Marginal ectasia of the cornea.** Klin. Monatsbl. f. Augenh. **128**:340-344, 1956.

Bilateral marginal ectasia was seen in a 56-year-old man who had had a chronic conjunctivitis for 15 years. Bacteriologic examination revealed the diplobacillus of Petit as the causative agent and it is assumed that this organism also caused thinning of the cornea. (3 figures, 26 references) Frederick C. Blodi.

Norn, M. S. **Cytology of conjunctivitis.** Acta Ophth. **34**:105-112, 1956.

The literature in this field is reviewed, and the author's own investigations reported. His material comprises conjunctival secretions of 305 patients. The specimens were taken with a dry cotton swab from the palpebral conjunctiva and from the edge of the closed lids. The specimens were stained with Giemsa stain. The cells found in the various types of conjunctivitis are tabulated. The most predominant type was the conjunctival epithelial cell. Neutrophilic leucocytes occurred in half the cases. Lymphocytes, histiocytes, and erythrocytes were seen less frequently, and eosinophilic and basophilic leucocytes were very rare. Acute infectious conjunctivitis was characterized by the presence of neutrophilic leucocytes, and often there were also erythrocytes, lymphocytes, and histiocytes. In ulcerative blepharo-conjunctivitis neutrophilic leucocytes and erythrocytes were found in the palpebral edges. In allergic conjunctivitis eosinophilic and basophilic leucocytes were seen in a relatively small number of cases. Chronic conjunctivitis was often associated with the presence of Pityrosporum ovale in the palpebral edges. The author concludes that cytological study is not of great diagnostic significance, and is indicated only in the clinically uncertain cases, and in those which do not respond to treatment. (2 tables, 19 references) Ray K. Daily.

Proptopopov, S., and Galchin, S. **The use of ethylcellosolf in the treatment of trachoma.** Vestnik offal. **1**:34-36, Jan.-Feb., 1956.

Ethylcellosolf or monoethyl ether of ethylenglycol acts as a "conductor" into the deeper tissues of various therapeutic liquids. Its action in various strengths was first tried on rabbits' eyes. In 45 patients with trachoma in stages 1, 2, and 3, ethylcellosolf in combination with antibiotics was used in the form of instillations into the conjunctival sac and in ointment form during a few weeks. It was found that the period of the transition into trachoma in its fourth stage was shortened as compared with the control eyes in which ethylcellosolf was not applied. Olga Sitchevska.

Rugiero, H. R., Halperin, L. and Arouh, J. **Primary tuberculous infection of the conjunctiva.** Arch. oftal. Buenos Aires **30**:485-490, Dec., 1955.

The case of a seven-year-old girl is presented, in whom an ulcerative and granulomatous lesion of the left upper tarsal conjunctiva existed in association with severe swelling of the homolateral preauricular and submaxillar lymph nodes. After a lapse of a few weeks, and in spite of systemic administration of large doses of streptomycin, the ganglia broke through the skin and expelled caseous material, in which direct bacterioscopic examination revealed the presence of the Mycobacterium tuberculosis. As soon as treatment was shifted to isonicotinyl hydrazide, the fistulas were seen to heal, the adenopathy improved and the conjunctival lesions disappeared. The patient's general condition remained unaffected during the whole process. (2 figures, 12 references) A. Urrets-Zavalia, Jr.

Thompson, M. and Eadie, S. **Keratoconjunctivitis sicca and rheumatoid arthritis.** Ann. Rheumat. Dis. **15**:21-25, March, 1956.

The most common ocular complication of rheumatoid arthritis is keratoconjunctivitis sicca, which occurred in 14 percent of the patients in the authors' series of 210 patients. In mild cases either a methylcellulose preparation or cortisone drops were prescribed with good results. For the more severe cases with actual corneal or conjunctival ulceration, diathermy coagulation of the lacrimal puncta was performed. (2 figures, 2 tables, 15 references) David Shoch.

Victoria, V., Galindez, J. and Gordillo, C. H. **Sjøgren's syndrome.** Arch. oftal. Buenos Aires **30**:493-505, Dec., 1955.

This is a detailed review of the literature on keratoconjunctivitis sicca. Current ideas on the subject are discussed and four cases presented, two in men (aged 26 and 31 years) and two in women (aged 32 and 53 years). (40 references)
A. Urrets-Zavalia, Jr.

Zurabov, G. **The prophylaxis of symblepharon in burns of the eye by paraffin paper.** Vestnik oftal. **1**:22-25, Jan.-Feb., 1956.

Zurabov offers a simple method of preventing the formation of symblepharon in burns of the eyes. He used it with good results in four patients. Sterilized double-folded wax or paraffin paper, cut to the size of the lid is inserted into the conjunctival sac. One wide mattress suture is applied to the lower lid and two to the upper lid. The sutures are brought out to the skin side on each lid. Vasoline or albucid ointment is inserted three times a day. The paper is softened by the tears and adheres closely to the conjunctiva of both lids, does not prevent the movement of the eyeball, the paper does not cause discomfort and allows slow drainage from the injured surface of the burn. In all patients the conjunctival sac was reformed. Olga Sitchevska.

8

UVEA, SYMPATHETIC DISEASE, AQUEOUS

Amsler, M., Verey, F., and Hubert, A. **The aqueous and its physiology.** Bull. et mém. Soc. franç. d'opht. **68**:1-39, May, 1955.

This very important study on the aqueous represented the principal paper of the sixty-second meeting of the French Ophthalmologic Society. It will be published in book form at a later date, as is customary.

A brief historical review summarizes the work of Leber in 1873, and emphasizes the significance of the discovery of the aqueous veins in 1942 and of the diagnostic punctures of the anterior chamber as performed during the last years. The aqueous should not be considered as the content of the anterior chamber only, but as the interstitial fluid of the whole eye. It has three main roles: regulation of the intraocular pressure, metabolism, and protective reaction to various stresses and insults. The term rheology (movement of fluid substances) as used by biologists is explained and the circulation of the aqueous is described as a typical rheological phenomenon. In the part devoted to the normal aqueous, problems relating to intraocular pressure, aqueous veins, and episceral venous plexuses are discussed, as are also the newer theories on the origin and outflow of the aqueous, the metabolic role of the aqueous as investigated by means of such methods as microelectrophoresis, chromatography and the specific isotopes, the characteristics of the blood-aqueous barrier, the dynamics of the aqueous as a continuously changing humor, and the effects of ascorbid acid, the various electrolytes and bicarbonates. A second section deals with the pathological aqueous, the secondary aqueous, anterior chamber puncture, studies of the inflammatory aqueous, bio-

microscopy, and the clinical significance of the fluorescein test.

Alice R. Deutsch.

Aranha de Azevedo, Paulo. **Etiology of uveitis.** Arq. brasil. de oftal. **18**:1-60, 1955.

The author discusses the etiology of uveitis comprehensively. The problem of onchocercosis in Brazil is more serious than we here in the United States realize. It apparently ranks second to trachoma as a cause of blindness, and is all the more important as no effective treatment is known which acts directly upon the filaria. The only effective measures are prophylaxis and surgical extirpation of the nodules. Diagnostic points of value are the presence of subcutaneous nodules, acute blepharospasm, photophobia, lacrimation and ciliary injection and superficial keratitis of a punctate variety. Slit-lamp examination reveals a uveitis and may allow observation of microfilaria in the tissues or anterior chamber.

The subject of endogenous uveitis is quite complex. Specific disease entities in which uveitis may be observed are summarized. There are tuberculosis, syphilis, leprosy, leptospirosis, brucellosis, gonorrhea, streptococcal infections, and toxoplasmosis. Other possible causes are sarcoidosis, herpes, rickettsial infection, lymphogranuloma venereum, and others. The value of puncture of the anterior chamber and examination of the aqueous is not generally appreciated by most ophthalmologists. Unfortunately, in many cases, the etiology will remain obscure after a thorough investigation. (83 references) James W. Brennan.

Schlaegel, T. F., Jr. and Salle, W. T. **Syndrome of purulent conjunctivitis, marginal keratitis, and severe non-granulomatous iridocyclitis.** Indiana St. M.A.J. **49**:259-262, March, 1956.

Seven cases are reported of a syndrome which consist of: 1. acute, severe, purulent, coagulase-positive staphylococcic conjunctivitis, 2. marginal keratitis with ulcer formation, 3. severe nongranulomatous iridocyclitis with a heavy aqueous flare and, in most cases, a gelatinous coagulum which nearly fills the anterior chamber. (1 table, 3 references)

Irwin E. Gaynon.

Temple Smith, E. **A method of iridotomy.** M. J. Australia **1**:738-739, May 5, 1956.

The author describes a method of iridotomy which he has used in cases of drawn-up pupil. A horizontal keratome incision is made in the 6-o'clock position, 3 mm. above the limbus. A Graefe knife is introduced, and a hole is made in the iris. This hole is enlarged with scissors vertically. (1 figure, 1 reference)

Hugh Ryan.

9

GLAUCOMA AND OCULAR TENSION

Bennet, George. **Surgical prognosis in glaucoma simplex.** Acta Ophth. **34**:73-91, 1956.

Believing that the fault of most statistics on glaucoma lies in an inadequate period of observation, Bennett analyzes the carefully scrutinized histories of 132 patients with simple glaucoma operated upon, with normalization of tension, at the Southhampton Eye Hospital over a period of 12 years. The minimum follow-up period was one year. The data are tabulated to exhibit 21 various relationships perspicuously. In certain selected cases of chronic glaucoma simplex in which a filtration operation was successful in over 60 percent of the patients, further visual failure occurred during the one to 16 years of observation. The series contained a significant preponderance of male patients and more than half of the

eyes sustained a severe loss of vision, which was greatest in the decade after 60 years of age. The outcome was, in general, independent of the age at which the operation was done except that iridencleisis was more successful in patients younger than 60 years. The prognosis was better in males than females among the very young and the very old and deteriorates increasingly with age. The eyes in which the tension was controlled by the use of miotics only, have a better prognosis than those which are treated surgically. (21 tables, 22 references) Ray K. Daily.

Bennett, George. **Surgical prognosis in congestive glaucoma; comparison with glaucoma simplex.** Acta Ophth. **34**:92-104, 1956.

This study of 44 eyes with congestive glaucoma is similar to one by the same author abstracted above. The arrangement of data is displayed in 12 tables. Again 60 percent of eyes showed further visual loss one to 15 years later. The highest incidences occurred in the decade after 60 years of age in both sexes. The prognosis does not vary with sex, the type of operation, the severity of visual loss, or with the age at operation. Acute glaucoma differs from chronic in that it is more common in women, is less severe at operation, the eye not treated surgically is better, and the degree of visual loss found at the time of operation does not increase with age. Eyes with acute and chronic glaucoma deteriorate visually at about the same rate; each fails by the fourteenth year. There is a 2:1 preponderance of males in chronic glaucoma and of females in acute. (1 figure, 12 tables, 12 references)

Ray K. Daily.

François, J. and Neetens, A. **Ocular hypertension and ophthalmic zona.** Acta Ophth. **34**:35-45, 1956.

Two cases are reported in which subacute homolateral ocular hypertension set in six to fourteen days after the appearance of the cutaneous vesicles, and two to four days before the onset of signs of iridocyclitis. Cases in which ocular hypertension precedes the onset of iridocyclitis are rare; 35 have been reported. An analysis of the symptoms in these cases and in those of the author suggests that the hypertension is not a manifestation of narrow-angle glaucoma, but of a hypertensive uveitis with an open iridocorneal angle, responding favorably to adrenaline. The cause of the hypertension is an increased production of aqueous due to the inflammatory congestion of the ciliary body, as well as an increase in the resistance to its outflow. The increased resistance is caused by a forward push of the iris and a diminution in depth of the anterior chamber, resulting from a congestion of the ciliary body and an accumulation of aqueous in the posterior chamber. The effect of adrenaline is a diminution in ciliary congestion and production of aqueous, leading to an increase in the depth of the anterior chamber, and a diminution in the resistance to outflow. In one of the patients tonography was performed during the rise in ocular tension, when the anterior chamber was 2 mm. deep. A second tonography was performed when the tension was lowered and the anterior chamber was 2.5 mm. deep, and a third when the tension was normalized, and the chamber was 3 mm. deep. The table of the resistance to outflow at these three different times shows a definite correlation between the resistance and the depth of the anterior chamber. Most investigators in the field of glaucoma hold that the depth of the anterior chamber and the degree of opening of the angle are not factors in the etiology of acute intraocular hypertension and that only complete closure of the angle can give rise to an acute rise of

intraocular pressure. The authors' laboratory experiments on rabbits have shown that the depth of the anterior chamber is a factor in the resistance to outflow, and that it rises in proportion to the diminution in the depth of the chamber. The tonographic data in the authors' case confirm these fiindings. The authors believe that in assessing tonographic results it is important to consider the depth of the anterior chamber. (3 figures, 60 references) Ray K. Daily.

François, J., Rabaey, M. and Neetens, A. **Perfusion in vitro of ten glaucomatous eyes.** A.M.A. Arch. Ophth. **55**:488-502, April, 1956.

The authors have shown by in vitro India ink perfusion in open, closed and secondary glaucoma that the obstruction to outflow is in or near the trabeculum. This article lends support to their previous article in which they state that the facility of aqueous outflow is in direct proportion to the depth of the anterior chamber. (17 figures, 1 reference) George S. Tyner.

de Gaspare, P. F. Ferraris. **Antiglaucoma operations in patients with cicatricial trachoma.** Ann. di. ottal e clin. ocul. **81**:545-562, Dec., 1955.

Elliot's trephining as well as Lagrange and Foroni operations are not very successful in cases complicated by cicatricial trachoma because of the frequent complete closure of the filtration scar. In acute glaucoma Graefe's iridectomy gives good results. Iridencleisis and cyclodialysis are effective, particularly the former. After iridencleisis normal tension was maintained even when the filtration scar became obliterated by scar formation. (7 tables, 28 references) John J. Stern.

Jaffe, N. S. and Light, D. S. **Flattened anterior chamber causing total anterior synechia and glaucoma.** A.M.A. Arch. Ophth. **55**:506-508, April, 1956.

Aphakic glaucoma due to closure of the angle by adhesion of the iris to the cornea was relieved surgically by making a suprachoroidal approach to the anterior chamber as in cyclodialysis and mechanically separating the iris from the cornea with a cyclodialysis spatula. (1 reference) George S. Tyner.

Maggiore, Luigi. **Iridencleisis in the surgical treatment of chronic glaucoma. The histologic basis of its mechanism of action.** Ann. d'ocul. **189**:152-162, Jan., 1956.

In albino rabbits, incarcerated iris pillars are quickly invaded by connective tissue and replaced by dense scar. Similar results occur after the inclusion of celluloid or mica lamellae. To prevent connective tissue proliferation after iridencleisis, it is necessary that pigmented cellular elements be incarcerated. (3 figures, 2 references) John C. Locke.

Palamarchuk, G. **The dynamics of the blind spot in glaucomatous patients under the influence of intravenous injections of sodium bromides.** Vestnik oftal. **1**:38-39, Jan.-Feb., 1956.

Campimetric studies of the size of the blind spot in 20 glaucomatous patients were made; 15 of the patients had questionable glaucoma, 3 had definite glaucoma and 2 had absolute glaucoma in one eye and initial glaucoma in the other.

In all patients intravenous injections of a 10 percent solution of sodium bromide were given. The size of the blind spot was studied by campimetry before the injection and one half hour, one hour, three hours, and one to seven days after the injections. The study was done mostly on patients with initial glaucoma because the process of the enlargement of the blind spot is still reversible. It

was found that the size of the blind spot decreases in the first hour after the intravenous injection of sodium bromide and usually to normal size. The duration of the action of sodium bromide fluctuated from three hours to seven days, the average being from three to five days. The individual duration of the action of the bromides on the blind spot indicates the neuro-reflectory mechanism of the process. (2 figures) Olga Sitchevska.

Tikhomirov, P. and Ustinova, E. **The simplification of the campimetric water drinking test.** Vestnik oftal. **2**:22-24, March-April, 1956.

A number of patients with definite or suspected glaucoma were given the water drinking test in the amount of 500 cc., 200 cc., 150 cc., and 100 cc. The blind spot was increased in the vertical diameter to about five degrees in 49 out of 50 eyes when 500 cc. of water was given, and in 43 out of 49 eyes when 200 cc. of water was given, but it was not changed by 200 or 150 cc. of water. It seems that 200 cc. of water is sufficient for producing the changes of the blind spot and it is safer to use the smaller amount of water in aged patients, particularly those who suffer from cardiovascular disease. (2 tables) Olga Sitchevska.

10

CRYSTALLINE LENS

McLean, John M. **Lens and vitreous.** A.M.A. Arch. Ophth. **55**:548-564, April, 1956.

The year's literature is reviewed. (173 references) George S. Tyner.

Páez Allende, Francisco. **Prolonged akinesia of the orbicularis muscle in cataract surgery.** Arch. oftal. Buenos Aires **30**:480-482, Dec., 1955.

Two to three cc. of 1 percent procaine 5-percent butyl aminobenzoate, in an aqueous excipient containing polyethylene glycol, propylene glycol and sodium metabisulphite, produced a temporary paralysis of the orbicularis which lasted for as long as six to eight days when injected near the outer canthus. The area was previously anesthetized with 6 to 8 cc. of a standard aqueous solution of 2-percent procaine hydrochloride, according to Van Lint's method. Forty-eight patients, among which there were some small children with congenital cataracts, were submitted to the above procedure with good results and no untoward local or general reaction. All of them were unusually free from blepharospasm.

A. Urrets-Zavalia, Jr.

Pearlman, Maurice D. **Prophylactic subconjunctival penicillin and streptomycin after cataract extraction.** A.M.A. Arch. Ophth. **55**:516-518, April, 1956.

A comparison is made of the incidence of postoperative purulent injection in patients receiving prophylactic subconjunctival antibiotics and those without the drugs. The author believes there is a significant reduction in the incidence of infection to warrant the routine use of these drugs. (2 tables, 9 references)

George S. Tyner.

Rossi, Pedro. **Ectopia lentis.** Arq. brasil. de oftal. **18**:61-68, 1955.

Ectopia lentis may be associated with other anomalies of the eye or of the body in general. Heredity is believed to play a role in its genesis. Possible causes are liquefaction of the vitreous, defects of the zonule, and developmental defects involving the lens, hyaloid system, and vascular capsule of the lens. There may be a simple dislocation of the lens, or the disturbance may be associated with corectopia, aniridia, colobomata, microphthalmos, or other visceral defects. The association with arachnodactyly is well known (Marfan's syndrome). The dis-

placement may remain static or be progressive in degree with the subsequent appearance of choroidal atrophy, vitreous opacities and complete dislocation.

Refraction is usually myopic in the phakic portion of the pupil and hypermetropic in the aphakic portion. Amblyopia of some degree is present, and strabismus may be observed. Treatment may be surgical or conservative, in which case the best possible vision is maintained by careful and frequent refraction. Two case histories are presented in which the author employed lens extraction after previous mydriasis. Final visual results are not reported. (14 references)

James W. Brennan.

11

RETINA AND VITREOUS

Ditzel, J. and White, P. **Central retinal vein occlusion in juvenile diabetes.** J. Chronic Diseases **3**:253-263, March, 1956.

The case history of a 15-year-old diabetic with a sudden occlusion of the central retinal vein is presented. This tragic occurrence in one eye was followed shortly by a proliferating retinopathy in the other. The authors feel that both diabetic retinopathy (microaneurysms and punctate hemorrhages) and central retinal venous occlusion are the result of protracted stasis in the venules. This generalized condition, they point out, is often well seen in the conjunctival venules and capillaries of the diabetic. The stasis is a result of venous distention and arteriolar narrowing which results in localized areas of ischemia and mural degeneration. The latter then causes the typical microaneurysm seen in diabetics and in cases of central retinal vein occlusion. (1 figure, 40 references)

David Shoch.

de Gaspare, P. F. Ferraris. **The behavior of Goldman's skiascotoma after operations for detached retina.** Ann. di. ottal. e clin. ocul. **81**:587-606, Dec., 1955.

In 23 patients successfully operated upon for detached retina (Weve's method) the activity of the perimacular retinal receptors showed a certain functional deficit. Goldman's skiascotoma demonstrated this disturbance, which was more pronounced in high myopia, in detachment of long standing and in detachments involving the macula. (23 figures, 12 references) John J. Stern.

Mikuni, M. and Ibarbaki, Y. **Clinical experiences with Padutin (Bayer) in central vein thrombosis.** Klin. Monatsbl. f. Augenh. **128**:323-332, 1956.

Five patients with thrombosis of the central vein or vitreous hemorrhage were successfully treated with Padutin, a hypotensive drug. The caliber of the retinal vessels was measured with an attachment to the Gullstrand ophthalmoscope. It could be seen that Padutin caused a marked vasodilatation. (5 figures, 1 table, 5 references) Frederick C. Blodi.

Schwab, F. **Fundus changes in tuberous sclerosis.** Klin. Monatsbl. f. Augenh. **128**:257-297, 1956.

Out of seven patients with tuberous sclerosis observed during the last two and one-half years five showed retinal tumors. The youngest patient was two and one-half years of age, the oldest 32. One patient had also a tumor of the disc and in the fundus of three chorioretinic scars could be seen. In addition 60 cases of the literature were analysed. (3 figures, 4 tables, 71 references)

Frederick C. Blodi.

12

OPTIC NERVE AND CHIASM

Hanbery, John W. **Glioma of the optic nerve.** Stanford Med. Bull. **14**:34-50, Feb., 1956.

In this excellent article the author points out that the most common primary tumor of the optic nerve is a glioma and that 90 percent of these occur before the age of 20 years. It is, therefore, the first thing to be thought of in unilateral exophthalmos in young adults. It can be differentiated from other lesions of the orbit by the early and profound loss of vision and the associated papilledema. The author, a neurosurgeon, advocates the transfrontal approach to these lesions. This is unquestionably the correct one since most of these tumors extend posteriorly and only in rare cases is the neoplasm confined to the intraorbital portion of the nerve. The prognosis in those cases without intracranial extension is excellent while almost all patients with such an extension succumb in several years. An excellent discussion of the microscopic anatomy of these tumors is appended. (6 figures, 31 references) David Shoch.

Krakau, C. E. T. **Papillary protrusion measurements by means of stereographs of the fundus.** Acta Ophth. **34**:140-145, 1956.

The author describes an apparatus to be used in connection with the Nordenson fundus camera for the purpose of making measurements of the changes in the level of the optic disc. It is emphasized that the absolute value of the protrusion is of limited significance as compared with the value of the difference between repeated measurements at different times. (5 figures, 5 references)
Ray K. Daily.

Wolter, J. R. and Liss, L. **Histopathologic changes of the optic nerve produced by direct compression.** Klin. Monatsbl. f. Augenh. **128**:297-306, 1956.

Two cases are described in which the optic nerve was compressed by a tumor. The excised optic nerves were stained with a modified Hortega silver stain. First an irritation of the astrocytes with reversible damage to the nerve fibers is found. Then follows hypertrophy and proliferation of the astrocytes with irreversible damage to the nerve fibers. Finally, there is also a breakdown of the astrocytes with connective tissue proliferation. (10 figures, 19 references)
Frederick C. Blodi.

13
NEURO-OPHTHALMOLOGY

Beck, A. T. and Guthrie, T. **Psychological significance of visual auras: study of three cases with brain damage and seizures.** Psychomatic Med. **18**:133-142, March-April, 1956.

The authors investigated the visual auras preceding grand mal seizures in three subjects. By use of hypnosis, "free association," and other psychiatric techniques, they were able to show that the auras are not simply manifestations of disease in the occipital or frontal lobe, but rather that the specific aura seen by a patient with brain damage represents a crucial personal problem of which the patient is unconscious normally. In a sense the visual aura is analagous to dream content. (1 table, 22 references)
David Shoch.

Dubois-Poulsen, A. and Magis, C. **Pathogenesis of Bjerrum's scotoma.** Ann. d'ocul. **189**:174-185, Feb., 1956.

Bjerrum's scotoma may be either a true scotoma or a depression in the middle isopters, the so-called baring of the blind spot. It is always negative and connected to the blind spot. It is not related to ocular tension and may be modified by medicaments such as caffeine, carbon dioxide, oxygen, pilocarpine and water intake. It is not confined to glaucoma; it is also found in choroiditis, choroidosis, diseases of the optic nerve and chiasm, and retrogeniculate lesions. The cause of the sco-

toma therefore must be in a well separated nerve-fiber bundle posterior to the eye itself, either near the globe (from a lesion of Haller's arterial circle) or farther back in the optic nerve or chiasm. (4 figures) John C. Locke.

Erausquin, H., Oribe, M. and Zimman, J. **Diagnostic role of cerebral angiography in neuroophthalmic syndromes.** Arch. oftal. Buenos Aires **31**:11-39, Jan., 1956.

In addition to a broad outline of the anatomy of the cerebral vessels and to a note on the current technique of carotid arteriography and of its complications, the authors present a detailed review of the features of diverse intracranial and intraorbital conditions, both from a clinical and from a radiological standpoint. Aneurisms, tumors and thromboses are discussed, special emphasis being laid upon their oculomotor, ophthalmoscopic and campimetric signs and symptoms, and 28 illustrative case records summarized. (19 figures, 57 references) A. Urrets-Zavalia, Jr.

François, J., Haustrate, L. and Philips, A. **Unilateral hydrophthalmos and homolateral facial hypertrophy.** Ann. d'ocul. **189**:186-202, Feb., 1956.

The authors present a case of unilateral buphthalmos associated with ipsilateral progressive hemihypertrophy of the face. Neurofibromatosis was suggested by the presence of cutaneous pigmented spots (café au lait spots) and a dissolution of continuity at the level of the lesser wing of the sphenoid bone, revealed by X-ray study. The diagnosis was confirmed by histological examination of swellings in the upper lid and soft tissues of the face (plexiform neuromata). (10 figures, 1 table, 42 references) John C. Locke.

Taveras, J. M., Mount, L. A. and Wood, E. H. **The value of radiation therapy in the management of glioma of the optic nerves and chiasm.** Radiology **66**:518-528, April, 1956.

The authors report 34 gliomas of the optic nerve and chiasm treated primarily with radiation. Results have been surprisingly good. In about half the patients there was arrest of visual loss and even restoration of the loss in some cases. This is, of course, unobtainable with surgical therapy. As a general principle the authors feel that surgery is indicated only for diagnostic purposes or to relieve obstruction of the cerebrospinal fluid and perhaps when the tumor is confined to one optic nerve and complete removal is possible. All other subjects with intracranial extension should have radiotherapy. The usual dose used is 800 to 1500 r given two to three times over a period of several months.

David Shoch.

Toussaint, D. **Preliminary notes on a comparative study of nocturnal and diurnal visual fields in neuro-ophthalmology.** Ann. d'ocul. **188**:1076-1112, Dec., 1955.

The author presents a comparative study of the visual fields of 64 patients having chiasmal or retrochiasmal lesions of the visual pathways. A greater sensitivity for nocturnal campimetry is noted. This is most marked at the time of onset of the field defect and during its regression. (24 figures) John C. Locke.

14

EYEBALL, ORBIT, SINUSES

Bertelsen, Torstein I. **The difference in exophthalmometric values on the two eyes in persons with a high degree of myopia in one eye.** Acta Ophth. **34**:69-72, 1956.

The material for this investigation comprises 36 anisometropes, with myopia in one eye. The difference in refraction of

the two eyes varied from 3 to 16 diopters, averaging 7.8 diopters. 22 patients had myopic fundus changes, and 14 did not. The tabulated data show that the increase in the length of the eye in axial myopia influences the exophthalmometric values differently, depending on whether myopic fundus changes are present or not. In the presence of myopic fundus changes the elongation of the eyeball is principally backward into the orbit, the anterior portion of the eyeball remaining unchanged; there is, therefore, but little change in the exophthalmometric value. In cases without myopic changes the elongation is mostly anterior, and the increase in the length of the eyeball is manifest by an increased exophthalmometric value. The author suggests that the tonus of the rectus muscles prevents a forward displacement of the eyeball when the eyeball is elongated only behind. (1 table, 6 references)

Ray K. Daily.

Otto, Joachin. **Clinical observations in malignant exophthalmus.** Klin. Monatsbl. f. Augenh. **128**:306-322, 1956.

Seven patients with malignant exophthalmus are described. In one case malignant exophthalmus occurred with hyperthyroidism. Medical thyroidectomy aggravated the situation and corneal ulcers developed. Slow improvement occurred after irradiation of the pituitary. In a second case malignant exophthalmus followed thyroidectomy. The BMR was low but no other thyroid function tests were done. Corneal ulcers developed. The patient was given di-iodotyrosin but the exophthalmus did not regress. Finally, both orbits were irradiated and slow improvement followed. In another case a biopsy was performed on one of the extraocular muscles. A hyaline-like deposit was found between sarcolema and contractile fibrils. Vitamine A or intraorbital hyaluronidase were of no value. In desperate cases an irradiation of the orbit (3000 r) is advised. Cataracts developed in one patient who was so treated, but they could be extracted without complications. (12 figures, 36 references)

Frederick C. Blodi.

Prado, Durval. **Operation of Damel.** Arq. brasil. de oftal. **18**:76-80, 1955.

A socket may not retain a prosthesis for several reasons, such as pressure from the weight of the shell, with resulting irritation and secretion, contraction of the tissues and loss of the inferior fornix. Catarrhal inflammation and profuse discharge are commonly observed. When the inferior cul-de-sac is shallow or absent, surgical reconstruction is indicated.

The author prefers to reconstruct the inferior fornix by using the conjunctiva of the socket, Damel's procedure. Briefly, this consists in a horizontal incision parallel to the lid margin, 6 mm. below it. The incision is deepened until the floor of the orbit is reached at the orbital margin. The fibrous and fatty tissue between the margin and the conjunctival fundus is removed. Double armed sutures are placed from the site of the desired conjunctival fornix, through the periosteum of the floor of the orbit at the inferior margin and emerge through the skin just below the skin incision. After these are tied, the skin incision is closed. Thus a fornix is constructed and is anchored to the orbital floor. (3 figures)

James W. Brennan.

15

EYELIDS, LACRIMAL APPARATUS

Bideau, R. and Levasseur, J. C. **Is lacrimal intubation so bad? Some results.** Ann. d'ocul. **189**:203-216, Feb., 1956.

Good results were obtained in 12 out of 16 patients treated over a one-year period by intubation of the nasolacrimal

duct with polyethylene tubing. The authors first slit the superior canaliculus. The canaliculus knife is then passed into the nasolacrimal duct, cutting edge forward, and rotated 180 degrees to sever the adhesions. The plastic tubing is then inserted on a double-bladed stylet. It is important to give systemic penicillin pre- and postoperatively. Two of the four failures were cases of postoperative infection with abscess formation in the sac, necessitating withdrawal of the tube. Neither had received penicillin preoperatively. A third occurred because the nasolacrimal duct was too narrow to permit insertion of the tubing. The final failure was due to an accident during the operation (formation of a false passage). The use of a special bayonet-shaped knife should prevent this in the future. Preoperative radiographic examination will eliminate those ducts which are too narrow for intubation. (6 figures, 49 references) John C. Locke.

Hanney, Franz. **Diagnostic X-ray studies of the lacrimal system.** Klin. Monatsbl. f. Augenh. **128**:336-340, 1956.

One-half cc. of a 40 percent Iodipin solution is injected. The films were taken in an anteroposterior direction with the patient lying down. In 90 percent of the 134 patients examined the sac was empty ten minutes after injection. (15 references) Frederick C. Blodi.

17
INJURIES

Koteliansky, E. **A perforating eye injury with eight cilia in the anterior chamber.** Vestnik oftal. **2**:36-38 March-April, 1956.

The patient, aged 23 years, had had an eye injury with glass three days before entering the hospital. The eye was acutely inflamed, the pupil was irregular. There were two wounds on the cornea at the 5- and 6:30-o'clock positions, the lens was opaque, and soft lens masses had prolapsed into the anterior chamber. Two shiny oblong foreign bodies, which were presumed to be glass fragments because of the history, were seen on the iris. An incision above the limbus was made with a keratome; the attempt to remove the foreign bodies with forceps was unsuccessful, so that a complete iridectomy was done and the soft lens masses were extracted. The foreign bodies proved to be cilia, two bunches with three cilia in each and one lump with two. It is important to remove cilia as soon as possible after the injury in order to prevent infection and secondary iridocyclitis and anterior chamber cysts.

Olga Sitchevska.

Martelli, A. and Strazzi, A. **Results of early surgical intervention in amauroses secondary to cranial trauma.** Riv. otoneuro-oftal. **31**:9-22, Jan.-Feb., 1956.

Exploration of the anterior cranial fossa followed by opening of the optic canal and nerve sheath was performed in six cases a few hours or days after skull injury. In two cases vision was improved to 20/500 and 20/200 respectively. Fracture of the optic canal was revealed by X-ray films in only one case, despite the presence of a bone lesion in three. Prompt use of this but slightly traumatic operation is recommended for prevention of possibly permanent injury to the optic nerve. (6 figures, 1 table, 7 references) G. Bonaccolto.

Wilkinson, J. A. **Traumatic hyphemia.** Louisiana St. Med. Soc. J. **108**:56-58, Feb., 1955.

Blood in the anterior chamber may be insignificant or it may be persistent and serious. The chief source is a tear at the root of the iris or iridodialysis. There is considerable difference of opinion as to the advisability of using a mydriatic to

rest the ciliary body or a miotic to increase the absorption of blood. The most frequent complications are secondary glaucoma and blood staining of the cornea. The treatment should consist of rest, sedation, and bandaging of the eyes. Should increased tension develop, a paracentesis should be done, followed by a miotic. Atropine is usually unnecessary. (6 references) Irwin E. Gaynon.

18

SYSTEMIC DISEASE AND PARASITES

Cucco, G. and Pende, G. **Fundus changes in plasmocytoma.** Ann. di ottal. e clin. ocul. **81**:477-493, Nov., 1955.

In ten cases a high incidence of fundus changes was observed. There were retinal hemorrhages and two types of deeper choroidal change reminiscent of either drusen or vacuoles ("oil-drops"). Thrombocytopenia, disturbances of coagulation time, hyperazotemia, and toxic endothelial lesions are probably responsible for the changes. (3 figures, 1 table, 9 references) John J. Stern.

Fornaro, Luigi. **Gastric function and blood crasis in alcohol-tobacco amblyopia.** Riv. oto-neuro-oftal. **31**:44-59, Jan.-Feb., 1956.

Detailed study of the gastric function, blood picture, and liver activity in patients with alcohol-tobacco amblyopia indicated that the histamineresistant achylia observed in 10 out of 12 cases is probably responsible for the complete deficiency of blood-regulating, vitamin, and nutritional factors which, in turn, causes both anemia and amblyopia. (1 table, 37 references) G. Bonaccolto.

François, J. and Verriest, G. **Developmental anomalies in children resulting from viral infections in the mother.** Ann. d'ocul. **189**:269-302, March, 1956.

The pertinent literature is reviewed and six new cases of rubella embryopathy with ocular involvement are reported. (4 figures, 266 references) John C. Locke.

Hedges, T. R., Jr., McAllister, R., Coriell, L. L. and Moore, W. **Metastatic endophthalmitis as a complication of meningococcic meningitis.** A.M.A. Arch. Ophth. **55**:503-505, April, 1956.

Two cases of endophthalmitis complicating meningococcic meningitis in infants are reported. The eyes of both appeared hopelessly ill with massive hypopyon. During systemic therapy with supportive local medical treatment no serious ocular sequellae developed. (3 references) George S. Tyner.

Reynon, M. and Masbernard, A. **The ocular fundus in acute porphyria.** Ann. d'ocul. **189**:319-428, March, 1956.

Severe hypertensive angiospastic retinopathy was observed in a case of acute intermittent porphyria. When the general signs of the disease receded, the fundi also returned to normal. The authors suggest that the neurological and other clinical manifestations may also be on a vasospastic basis, and that the fundus changes observed here occur more frequently than previously observed. (27 references) John C. Locke.

19

CONGENITAL DEFORMITIES, HEREDITY

Laitenen, L., Miettinen, P. and Sulamaa, M. **Ophthalmological observations in craniosynostosis.** Acta Ophth. **34**:121-132, 1956.

The literature is reviewed, and 29 cases briefly reported; in 22 of these treatment consisted of linear craniectomy. The tabulated data show the age, sex, the general symptoms, the obliterated suture, lumbar pressure, and the ophthalmological findings. Seventeen patients were

boat heads and four of them had ophthalmologic symptoms, and of twelve who had tower heads eight had ophthalmological symptoms. One third of the patients were less than one year old, and the oldest was eight years old. Four children in this series were brought to the clinic because of ophthalmological symptoms. The latter are due to the local deformity, to increased intracranial pressure, or to a combination of both factors. Increased intracranial pressure causes visual impairment through papillary stasis and optic atrophy. It is also the cause of exophthalmos. The treatment is surgical, and a linear craniectomy reestablishes the growth of bone, relieves the increased intracranial pressure, and checks further visual deterioration. Operation has a decidedly favorable effect on the papillary stasis; the vision of a boy who had been blind for two weeks was restored after surgery. The authors stress the importance of early surgery and consider the optimal age under six months. (5 figures, 4 tables, 28 references) Ray K. Daily.

Rizzo, Paolo. **Reflections on a case of Lawford's syndrome (Naevus flammeus of the face and chronic glaucoma without enlargement of the globe).** Ann. di. ottal e clin. ocul. **81**:607-620, Dec., 1955.

The literature is reviewed and a case described which was uusual in that it was complicated by anterior uveitis which developed within a few months into a hemorrhagic glaucoma. The cause for the hypertension in this syndrome is considered to be a vascular disturbance leading through consecutive attacks of uveitis to a reduction of the aqueous outflow. (3 figures, 67 references)

John J. Stern.

Sohar, Ezra. **Renal disease, inner ear deafness and ocular changes: a new heredofamilial syndrome.** Arch. Int. Med. **97**:627-630, May, 1956.

Four cases of a new syndrome are described, the ocular portion of which consists of a moderate myopia, spherophakia (in two cases) and posterior cortical cataracts (in two cases). The pedigree obtainable is too short to permit any conclusions as to type of transmission. The deafness is of the inner ear type and the renal disease a nonspecific chronic nephritis. (2 figures, 3 tables, 5 references) David Shoch.

Urrets-Zavalia, Alberto, Jr. **The peristomodeal malformations.** A.M.A. Arch. Ophth. **55**:526-545, April, 1956.

Some developmental malformations of the face coincident with ocular malformations are described and classified. Some of the accompanying eye conditions are paralytic squint, microphthalmia. and ptosis. (11 figures, 64 references)

George S. Tyner.

Westerlund, E. **Inheritance of choroideremia.** Acta Ophth. **34**:63-68, 1956.

Westerlund reviews the literature and reports three cases in fully developed form in men, and five cases of the intermediate form in female descendants, distributed over two families. There were two affected brothers in one family, and a solitary case in the other family. From a review of the literature, and an analysis of these cases, it appears that the inheritance of choroideremia is that of intermediate sex-linked dominance. The author believes that the seriousness of the affection justifies sterilization, and patients should be told about the risk involved for their descendants. Sons of choroideremic patients do not transmit the affection, but if the daughters show ophthalmoscopic signs of the disease they are transmitters, and fifty percent of their offspring, boys and girls, will carry the gene for the disease. The boys will become blind, and the girls will transmit the disease to their offspring.

In female transmitters who have no visual disturbances, the ophthalmoscope reveals a muddy appearance of the fundus, the result of displacement of choroidal pigment, grouped in small grains with a slight tendency to a radial arrangement and with no relation to bloodvessels. The pigment is denser in the equatorial region, decreasing in density towards the posterior pole. There is, also, fine pigmentation in the macula. (2 geneologic charts, 7 references) Ray K. Daily.

20

HYGIENE, SOCIOLOGY, EDUCATION, AND HISTORY

Kopp, I. and Satz, L. **Ambulatory service to glaucomatous patient in cities and regions of Stalin's District.** Vestnik oftal. 1:8-16, Jan.-Feb., 1956.

The Health Ministry of the U.S.S.R., since 1952, took measures for the improvement of the ambulatory service and for the early diagnosis of glaucoma in the cities and rural hospitals. The number of oculists was increased who were taking special courses in glaucoma. Information is broadcast by popular talks on glaucoma, discussions in newspapers and over the radio. The oculists from the larger cities make periodic visits to the rural districts for a check-up and instructions to the local physicians and nurses. As a result of this intensive education and control of glaucoma in this region, the observation of 564 patients showed that stabilization of initial glaucoma was obtained in 91 percent. (3 tables)

Olga Sitchevska.

Oliver, J. R. and Lauer, A. R. **Correlation of speed and distance judgment with visual acuity.** Am. J. Optometry **33**: 263-265, May, 1956.

Safe driving requires good judgment of the distance and speed of oncoming cars. For licensing, most states require only visual acuity tests. The authors indicate that drivers with reasonably good acuity may have poor distance and speed judgment. Of 108 subjects, half were men. The group was homogeneous enough that data were considered significant. The men were significantly more exact in tests estimating distance and speed of oncoming cars. Both men and women tested were experienced in driving. Paul W. Miles.

Ophthalmic Miniature

It is stated that he thought scarlet the most beautiful of all colours, and that he ranked the pleasure he derived from the others in proportion to their brilliancy and gaiety. The first time, indeed, that he saw black, it excited the greatest uneasiness in his mind, as if there was some intrinsic idea absolutely proceeding from the colour, and thus pointing out that certain colours have been adopted for the purpose of expressing certain ideas, instead of those ideas being implanted in the mind by association. Besides, it is well known that an intelligent blind man once compared his ideas of scarlet to the sound of a trumpet; and from such idea it was that Cheselden's patient could not, for some time, be reconciled to the colour of black; nay, after he was in some measure accustomed to it, he was struck with utmost horror at the accidental sight of a Negro woman.

H. Colburn, London, 1816.

NEWS ITEMS

Edited by DONALD J. LYLE, M.D.
411 Oak Street, Cincinnati 19, Ohio

News items should reach the editor by the 12th of the month. For adequate publicity, notice of postgraduate courses and meetings should be received three months in advance.

DEATHS

Dr. Clarence Porter Jones, Newport News, Virginia, died February 27, 1956, aged 81 years.

Johan George Raeder, Oslo, Norway, died June 10, 1956, aged 67 years. He was an ardent investigator and contributed extensively to ophthalmology. His most important article is the description of the paratrigeminal disturbance since known as Raeder's syndrome (Brain, **47**:149, 1924). He was trained under Professor Schiøtz and was one of his most brilliant students.

SOCIETIES

OXFORD PROGRAM

The following program was presented at the annual Oxford Ophthalmological Congress:

"Problems of lacrimal obstruction," openers: Mr. L. P. Jameson Evans, Birmingham, Mr. R. G. Macbeth, Oxford, and Mr. T. Keith Lyle, London; "Diagnostic conjunctival biopsy in sarcoidosis," Mr. R. Pitts Crick, London; "New aspects of the etiology of Sjøgren's syndrome," Dr. J. McLenachan, Birmingham.

"Surgical treatment in simple glaucoma," Mr. F. W. Law, London; "An exposition of ophthalmoscopic photographs," Dr. A. J. Bedell, Albany, New York; "Some principles in the surgery of retinal detachments," Mr. Rupert Parry, Cardiff; "Experimental ocular hypertension in animals," Mr. J. P. F. Lloyd and Dr. E. H. Leach, Oxford.

"Biochemical changes in radiation cataracts," Mr. A. Pirie, Oxford; "Defective color vision caused by eye diseases," Dr. W. Jaeger, Heidelberg; "Corneal graft fixation," Mr. D. Ainslie, London; "The later stages of retrolental fibroplasia," Mr. A. C. L. Houlton, Oxford.

"Plastic lens insertion into anterior chamber," Dr. J. Barraquer Moner, Barcelona; "Scleral plication for retinal detachment," Mr. E. F. King, London; "Ocular manifestations of general disease," Mr. J. Minton, London; "Monocular proptosis," Mr. D. P. Choyce, Southend; "Visual aids for the pathologic eye," openers: Mr. P. McG. Moffatt, London, Mr. D. Stenhouse Stewart, Hull, Mr. C. H. Keeler, London, and Mr. J. Pike, London.

"Sidelights on refraction," Mr. F. A. Williamson-Noble, London; "Some problems arising in a case of malignant melanoma of the choroid," Mr. O. Gayer Morgan, London; "Some clinical aspects on gonioscopy," Mr. W. J. W. Ferguson, Sheffield.

The Doyne Memorial Lecture was delivered by Prof. Robert Platt, Manchester, whose subject was "A physician's thoughts on the retina."

OFFICERS ELECTED

Officers for the Sociedade de Oftalmologia e Otorrinolaringologia do Rio Grande do Sul for 1956-57 are:

President, Dr. Paulo Fernando Estevos; vice-president, Dr. Jayme Schilling; first secretary, Dr. Carlos Buede; second secretary, Dr. Moizés Sabani; first treasurer, Dr. Israel Scherman; second treasurer, Dr. Rivadávia C. Meyer; librarian, Dr. Carlos M. Carrion.

ARGENTINE CONGRESS

On the executive council of the VI Argentine Congress of Ophthalmology are: Dr. Carlos S. Damel, president; Prof. Paulina Satanovsky and Dr. Nicolás Gonzalez Llanos, vice-presidents; Dr. Jorge Balza, Dr. Hector R. Pícoli, Prof. Juan M. Vila Ortiz, and Dr. Edgardo Manzitti, secretaries; Dr. Moisés Brodsky, treasurer; Dr. Estenban Adrogué, Prof. Raúl Argañaráz, Prof. Diego M. Arguello, Prof. Jorge L. Malbrán, and Prof. Alberto Urretz Zavalia, honorary presidents.

The congress will be held in Mar del Plata, Argentina, on April 9 to 14, 1957.

AOS OFFICERS

At its annual meeting, the American Ophthalmological Society elected the following officers for the current year:

President, Dr. Frederick C. Cordes, San Francisco; vice-president, Dr. Walter S. Atkinson, Watertown, New York; secretary-treasurer, Dr. Maynard C. Wheeler, New York; editor, Dr. Gordon M. Bruce, New York.

NEW YORK OFFICERS

The newly elected officers of the New York Society for Clinical Ophthalmology for the 1955-57 season are:

President, Dr. Max Chamlin; vice-president, Dr. Harvey E. Thorpe; recording secretary, Dr. Jesse M. Levitt; corresponding secretary, Dr. Leon H. Ehrlich; treasurer, Dr. Henry M. Kera; historian, Dr. Robert S. Coles.

Chairmen of the various committees are: Program, Dr. Abraham Schlossman; instruction sessions, Dr. Arthur Linksz; legislative, Dr. Benjamin

Rosenthal; membership, Dr. Howard Agatston; industrial, Dr. Edward M. Douglas.

Canadian officers

At the recent 19th annual meeting of the Canadian Ophthalmological Society, the following officers were elected:

President, Dr. John McLean, Vancouver; vice-president, Dr. J. V. V. Nicholls, Montreal; secretary, Dr. R. G. C. Kelly, Toronto; treasurer, Dr. Benjamin Alexander, Montreal; editor, Dr. Clement McCulloch, Toronto.

Military ophthalmologists

The Society of Military Ophthalmologists and the Society of Military Otolaryngologists will hold a joint stag dinner meeting at the time of the annual meeting of the American Academy of Ophthalmology and Otolaryngology in Chicago in October.

Dinner will be served at 6:30 p.m. on October 16, 1956, at the Palmer House. The dinner will be followed by a short business meeting.

All members of the Society of Military Ophthalmologists and the Society of Military Otolaryngologists are invited to attend. Application may be made to either Capt. James A. Stokes (MC) secretary-treasurer, Society of Military Ophthalmologists, Eye Clinic, Walter Reed Army Hospital, Washington 12, D.C. or to Maj. Stanley H. Bear (MC) 3810th USAF Hospital, Maxwell Air Force Base, Alabama.

Personal

The $250 prize for the best paper presented at the June meeting of the Section on Ophthalmology, A.M.A., was awarded by the executive committee to Dr. T. E. Sanders, St. Louis, for his paper, "Fundus keratitis." The award was judged on the basis of presentation and originality.

Ophthalmic Miniature

Joseph Priestley's "The History and Present State of Discoveries Relating to Vision," London, 1772, was translated into German by Georg Simon Kluegel, Ph.D. This German translation contains the first report in literature of a performance of Mariotte's experiment before the king of England. . . . The foundation of his note can only have originated in a footnote found in Albert v. Haller's *Elementa Physiologicae*, T. 5 p. 470 where mention is made of Mariotte's experiment, giving the following information:

Factum ann. 1668 coram S. Reg. Maj. T. Burch. T II p. 281. Exstat oper. Mariot. p. 496. ed Holl.

This apparently well-authenticated notice was incorporated in Helmholtz's *Physiologische Optik* without further inquiry. . . . The report that Mariotte showed his experiment to Charles II, king of England, must be a fiction originating in a misreading of an abbreviated Latin footnote in Haller's *Physiology*.

J. Brøns: *The blindspot of Mariotte.* Acta Ophth., 17:(Supplement p. 31), 1939.

Instruments of ophthalmology: *The Costenbader Childrens Trial Frame*

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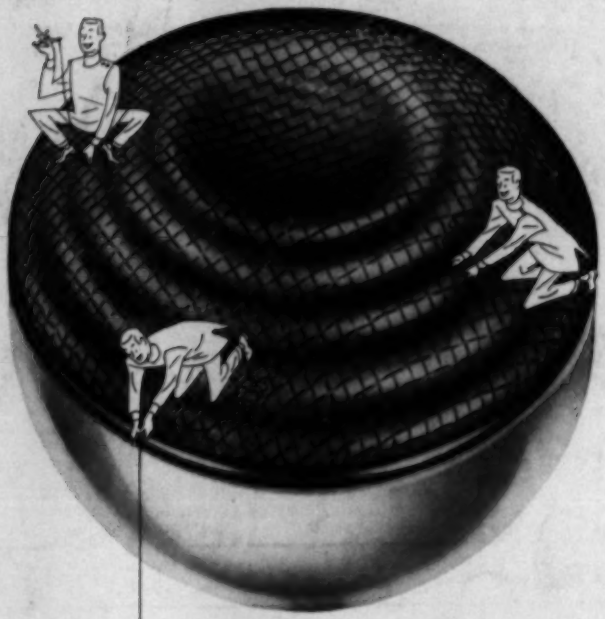

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